EXHIBIT AA

IN THE UNITED STATES DISTRICT COURT

FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA

CHARLESTON DIVISION

- - -

IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM, PRODUCTS LIABILITY LITIGATION	:MDL NO. 2327 : :VOLUME II :

THIS DOCUMENT RELATES TO ALL CASES AND VARIOUS OTHER CROSS-NOTICED ACTIONS

CONFIDENTIAL - SUBJECT TO PROTECTIVE ORDER

- - -

January 8, 2014

- - -

Transcript of the continued deposition of THOMAS A. BARBOLT, Ph.D., called for Videotaped Examination in the above-captioned matter, said deposition taken pursuant to Superior Court Rules of Practice and Procedure by and before Michelle L. Gray, a Certified Court Reporter, Registered Professional Reporter, and Notary Public, at the offices of Riker Danzig Scherer Hyland & Perretti LLP, Headquarters Plaza, One Speedwell Avenue, Morristown, New Jersey, commencing at 9:07 a.m.

- - -

GOLKOW TECHNOLOGIES, INC.
877.370.3377 ph| 917.951.5672 fax
deps@golkow.com

APPEARANCES:

AYLSTOCK, WITKIN, KREIS & OVERHOLTZ, PLLC
BY: DANIEL THORNBURGH, ESQUIRE
17 East Main Street, Suite 200
Pensacola, Florida 32502
(850) 202-1010
dthornburgh@awkolaw.com
Representing the Plaintiffs

THOMAS, COMBS & SPANN, PLLC
BY: DAVID B. THOMAS, ESQUIRE
BY: PHILIP J. COMBS, ESQUIRE
300 Summers Street, Suite 1380
Charleston, West Virginia 25301
(304) 414-1805
dthomas@tcspllc.com
pcombs@tcspllc.com
Appearing on behalf of the Defendants; Ethicon, Inc.; Ethicon Women's Health and Urology, a Division of Ethicon, Inc.; Gynecare; and Johnson & Johnson

APPEARANCES VIA TELEPHONE:

AYLSTOCK, WITKIN, KREIS & OVERHOLTZ, PLLC
BY: BOBBY J. (BRAD) BRADFORD, ESQUIRE
BY: D. RENÉE BAGGETT, ESQUIRE
17 East Main Street, Suite 200
Pensacola, Florida 32502
(850) 202-1010
rbaggett@awkolaw.com
Representing the Plaintiffs

FREEARK, HARVEY & MENDILLO, P.C.
BY: RANSOM P. WULLER, ESQUIRE
115 West Washington Street
Belleville, Illinois 62222
(618) 233-2686
rwuller@freeark.com
Representing Heartland Women's Healthcare, Ltd., and Dr. Elisabeth G. Beyer-Nolen

BONNE, BRIDGES, MUELLER, O'KEEFE & NICHOLS
BY: SUSAN FAYE L. FRANCISCO, ESQUIRE
3699 Wilshire Boulevard, 10th Floor
Los Angeles, California 90010
(213) 738-5842
sfrancisco@bonnebridges.com
Representing Gerald Thorpe, M.D.; Keller vs. Siddighi, et al., San Bernardino County Superior Court, case No. CIVDS1307951

VIDEOTAPE TECHNICIAN:

Lee Bittman

TRIAL TECHNICIAN:
Michael Andrews

- - -

- - -

I N D E X

- - -

- - -

E X H I B I T S (Cont'd.)

- - -

- - -

E X H I B I T S (Cont'd.)

- - -

- - -

E X H I B I T S (Cont'd.)

- - -

- - -

E X H I B I T S (Cont'd.)

- - -

- - -

E X H I B I T S (Cont'd.)

- - -

- - -

E X H I B I T S (Cont'd.)

- - -

- - -

- - -

DEPOSITION SUPPORT INDEX

- - -

Direction to Witness Not to Answer

PAGE LINE

None

Request for Production of Documents

PAGE LINE

423 3

Stipulations

PAGE LINE

None

Questions Marked

PAGE LINE

None

- - -

THE VIDEOGRAPHER: We're now on the record.

Today is January 8, Year 2014. It's 9:07 a.m.

This begins Volume 2, Tape Number 1 of the videotape deposition of Dr. Thomas A. Barbolt.

Please proceed.

- - -

... THOMAS A. BARBOLT, Ph.D., having been previously sworn, was examined and testified as follows:

- - -

CONTINUED EXAMINATION

- - -

BY MR. THORNBURGH:

Q. Good morning, Doctor.

A. Good morning.

Q. How are you doing this morning?

A. Very good.

Q. Another cold day in New Jersey?

A. It will change.

Q. Doctor, we talked a little bit about the IFU yesterday, and a statement that you were --

within the IFU, that you were designated as a witness to discuss.

Do you recall that IFU statement?

A. Yes.

Q. Go ahead and take out Exhibit Number 2246, which is the IFU that we marked yesterday.

THE VIDEOGRAPHER: Off the record.

(Brief pause.)

THE VIDEOGRAPHER: Back on the video record, 9:10.

BY MR. THORNBURGH:

Q. Doctor, do you have Exhibit Number 2246?

A. Yes.

Q. And do you recall that you had a discussion yesterday regarding this claim in the IFU?

The first claim is: Animal studies show the implantation of Prolene mesh elicits a minimal inflammatory reaction in tissues, which is transient, and can -- and is followed by the deposition of a thin fibrous layer of tissue, which can grow through the interstices of the mesh, thus incorporating the mesh into the adjacent tissue.

Do you recall that?

A. Yes.

Q. From yesterday, right?

A. Yes.

Q. And you had identified in Exhibit 2241 a list of -- I believe it was -- I'm sorry. Maybe we didn't mark it yesterday -- the IFU binder that you have in front of you.

Let's go ahead and mark both of those binders as exhibits.

We'll mark the first one as Exhibit Number 2248.

MR. THOMAS: Do you mind if I identify the volumes?

MR. THORNBURGH: Go ahead.

(Whereupon, a discussion was held off the record.)

MR. THOMAS: For the record, Volume 1 of the documents that have been provided to the plaintiffs in response to the notice of deposition for the language in the information for use just identified by counsel.

Exhibit 2248 is Volume 1, which contains Tabs 1 through 32 of those documents.

(Whereupon, a discussion was held off

the record.)
MR. THOMAS: Exhibit 2249 is Volume 2 of the studies which are responsive to the 30(b)(6) topic just discussed by counsel. And these are Tabs 33 through 34 produced by Ethicon and as documents upon which Dr. Barbolt relies in support of that designation.
(Document marked for identification as Exhibit T-2248.)
(Document marked for identification as Exhibit T-2249.)
BY MR. THORNBURGH:
Q. Okay. Now, Doctor, do you agree with me that this claim in the IFU says that animal studies show the implantation of Prolene mesh elicits a minimal inflammatory reaction in tissues which is transient. Right?
A. Yes.
Q. And it discusses in the first sentence, first part of that sentence, that the animal studies relate to Prolene mesh. Correct?
A. Yes.
Q. Okay. And in the -- in the documents that you submitted or the list that you submitted as part of exhibits numbered 2248 and 2249, the vast

majority of those are suture studies, right?
A. There are some suture studies in that list.
Q. Well, I said vast majority of those are suture studies, right?
A. I didn't make that assessment.
Q. Okay. Well, let's look at it real quick.
Your Tab Number 1 in Exhibit 2248 is a suture study, correct?
A. Yes.
Q. Tab 2 is a suture study, correct?
A. Yes.
Q. Tab 3 is a suture study, correct?
A. Yes.
Q. Tab 4 is a suture study, correct?
A. Yes.
Q. Tab 5, it says excerpt from NDA 16374, package insert, labeling approved 1969. That's also a suture NDA, correct?
A. Yes.
Q. The Postlethwait study that you have listed here isn't a study that you conducted, right?
A. This is a study from the open literature.

Q. Okay. And that study is related to sutures, right?
A. Yes.
Q. Suture packed with permeable labels. I assume that's a study, but that's a suture study, correct?
A. Yes.
Q. The next one is a epoxy-tipped nylon and Prolene biological evaluation.
That's also a suture document, isn't it?
A. Yes.
Q. The next tab in your notebook, excerpt from NDA 1634, that's just a repeat of what's up here, it appears, but from 1973, right, also suture?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yeah. It's a different version.
BY MR. THORNBURGH:
Q. A different version, but updated version from 1973 related to sutures, correct?
A. Yes, that's correct.
Q. The next document is the Prolene mesh

biological evaluation in rabbits, which is from 1973, which is the study that we ended talking about from yesterday, correct?
A. Yes.
Q. And in that study, it showed that there was chronic inflammation seen in all rats -- in all rabbits in that study at the end period of that study, at day 28, correct?
A. I would have to look at the specifics there, but there was the record of chronic inflammation in some rabbits at the 28-day time point.
Q. And, by the way, that rabbit study that you did that formed the basis of the claim in the IFU was a short-term study, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: It's a 28-day study.
BY MR. THORNBURGH:
Q. That's considered in the laboratory science field to be a short-term study, tissue reaction study, correct?
MR. THOMAS: Objection.
THE WITNESS: Yes.
BY MR. THORNBURGH:

Page 311

Q. The next study that you have listed in that binder is a Prolene polypropylene suture tissue response. That's another suture study, correct?
A. Yes.
Q. The following study is a suture study, correct?
A. Yes.
Q. Then there's another publication from Postlethwait, which is also related to sutures, correct?
A. Well, I see Tab 14 is not the Postlethwait. That is the next one in the list.
Q. Well, Tab 14 is suture. Tab 15 is suture, right?
A. Yes.
Q. Tab 16, Salthouse, that's a former employee of Ethicon, isn't it?
A. What was that? Tab 15?
Q. Yep.
A. Tab 15?
Q. The tab after Postlethwait.
A. Tab 14.
Q. You said it was 15 a moment ago. Let's go ahead and mark that as 14.

Page 312

Tab 15 is Salthouse, right?
A. 14 is Salthouse.
Q. Okay. Let's make sure we're on the same page here.
Tab 14. Salthouse is a former employee of Ethicon, right?
A. Yes, that's correct.
Q. And that's also a suture study, correct?
A. Yes.
Q. Tab 15 is another suture study?
A. Yes.
Q. Now, we can go through all these. I don't want to waste anybody's time here, but you'd agree with me that the vast majority -- the overwhelming majority of these studies that you listed are suture studies, correct?
MR. THOMAS: Objection to form.
THE WITNESS: I wouldn't make that statement unless I've gone through the exercise that you're doing. If you've done that, then I have no reason to doubt -- to doubt your conclusion.
BY MR. THORNBURGH:
Q. Well, we know from Tab 1 through 15 there's only one mesh-related study, right?

Page 313

A. Yes.
Q. And as the ladies and gentlemen can see, the document I am holding up, the remaining studies appear to be vast -- the vast majority of these studies are suture studies, right?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. Well, let's go through the exercise.
Tab 16, Ethilon and Prolene ocular tissue response. That's suture, right?
A. Yeah.
Q. The next document listed here is another suture study, right?
A. Yes.
Q. The following study is another suture study, correct?
A. Yes.
Q. The following study, size 5-0 and zero Prolene cobalt and ethylene oxide sterilized, effects of sterilization on tissue reaction.
That's -- is that -- that was not looking at mesh, was it?
A. That's a suture study.
Q. Right. And we're looking at the

Page 314

effects of EO, which is a sterility method, correct?
A. Yes. It is a sterilization method.
Q. The next study that you have listed here is another suture study that looked at Procol versus Lubrol, which are antioxidants, additives contained within the resin, correct?
A. Yes.
Q. Again, it's related to sutures, right?
A. Yes.
Q. Prolene -- the next study is another suture study, followed by another suture study.
Now we are at the FDA reclassification of Prolene polypropylene non-absorbable sutures.
That's related to sutures, right?
A. That's correct.
Q. The following study is a suture study, right?
A. Yes.
Q. Prolene polypropylene suture. That's another suture study, right?
A. Yes.
Q. Another suture study followed by that, right?

Page 315

A. Yes.
Q. Now we're at the Prolene suture dyed size stability study, Number 749. That's clearly a suture study, right?
A. Yes.
Q. Followed by the 91-day ophthalmic tissue reaction study in rabbits.
That's a suture study, right?
A. Yes.
Q. Followed by a one-month dural tissue reaction study of dyed NGP. That's a suture study, right?
A. Yes.
Q. 182, intramuscular tissue reaction study in rats is a suture study, right?
A. Yes.
Q. Followed by six-month dural tissue reaction absorption efficacy study of ETHISORB, which isn't even Prolene, is it?
A. That is a Dormier substitute for ETHISORB. This is the material that is part of TVT-S.
Q. It's not -- my question is very specific. Okay? It's a yes or no question.
ETHISORB is not Prolene, is it?

Page 316

A. That's correct.
Q. Then you have a 28-day intramuscular tissue reaction study in rats with polypropylene mesh from the TVT device.
That is a study we looked at yesterday that showed a moderate inflammatory response that was chronic, right?
MR. THOMAS: Objection to form of the question.
BY MR. THORNBURGH:
Q. I think it was described as a mild to moderate inflammatory response, which was chronic, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I think you're thinking of the autoclave study that we discussed yesterday --
BY MR. THORNBURGH:
Q. I'm sorry. I thought that's what we were looking at here.
So 28-day intramuscular tissue reaction study that we discussed briefly yesterday, that was a study to look at the cytotoxic effect of polypropylene, right?

Page 317

MR. THOMAS: Object to the form of the question.
THE WITNESS: To look at the tissue reaction, integration, and response.
BY MR. THORNBURGH:
Q. Well, it was looking at -- the specific endpoint in that study was looking at -- for necrosis to determine if the Prolene in the TVT was cytotoxic.
MR. THOMAS: Object.
BY MR. THORNBURGH:
Q. Right?
MR. THOMAS: Objection to form.
THE WITNESS: That's one of the endpoints of that study.
BY MR. THORNBURGH:
Q. Do you have that study with you?
A. Of course.
Q. All right. Why don't you pull it out and read what the purpose of that study was.
It should be in Tab 2 of your IFU.
A. I'll go to Tab 32 of my list of studies.
Q. I meant to say Volume 2.
A. I am looking on ETH.MESH.05315244,

Page 318

the protocol. The purpose of the protocol. The purpose of the study. The purpose of the study is to assess the tissue reaction of polypropylene mesh from the TVT (Ulmsten) device when implanted in rat gluteal muscle for up to 28 days and to compare this reaction to that elicited by current production Prolene polypropylene mesh.
Q. And you recall that that study was conducted after the TVT device tested severely cytotoxic by one of your laboratories in Ohio, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: To clarify, this study was conducted after an in vitro cytotoxicity test that showed -- in fact, there were two studies. One showed a moderate in vitro cytotoxicity, and the other showed severe in vitro cytotoxicity.
BY MR. THORNBURGH:
Q. So the reason that you had decided to conduct the study is to look at the in vivo cytotoxicity of the TVT device, correct?
A. Well, I just read the purpose of this experiment.
Q. Doctor, I don't -- Doctor, I mean --

Page 319

MR. THOMAS: Let him answer the question, please, Dan.
MR. THORNBURGH: Well, he's not answering the question.
MR. THOMAS: Yes, he is.
MR. THORNBURGH: He knows the answer. He's not being straightforward with the jury.
The reason that -- the reason why you have --
MR. THOMAS: Stop just a minute. Stop just a minute. Just a minute.
You're not going to characterize the witness's testimony for the jury or anybody. You can ask him questions.
MR. THORNBURGH: You can move to strike.
MR. THOMAS: If you --
BY MR. THORNBURGH:
Q. Doctor -- Doctor, you know. You are the -- you were the investigator at Ethicon who ordered that this study be conducted, right?
A. Yes.
Q. And you did it for the purpose of showing that the TVT device is not cytotoxic in vivo. That was the reason why you did it, right?

Page 320

A. The purpose of this study is as stated in the protocol, which is the overall direction of the study. And that purpose was to assess the tissue reaction of polypropylene mesh from TVT when implanted in rat gluteal muscle for up to 28 days.
Q. Were you not trying to determine whether or not the TVT device was cytotoxic in vivo in this study?
A. Any in vivo cytotoxicity related to TVT mesh would have been revealed during the conduct of this study in response to the purpose to the study.
Q. Another short-term study, correct, by definition in the laboratory scientific community?
A. This is a short-term experiment.
Q. Then you have the 182 intramuscular tissue reaction study in rats using polypropylene mesh with Triclosan.
That was after that statement had already been included in the IFU label, right?
After the statement -- after the statement that animal studies show the implantation of Prolene mesh elicits a minimal inflammatory reaction in tissue which is transient, right? That

Page 321

language was already in the IFU?
A. Yes. By 2000 that language was already in the IFU.
Q. And the purpose of that study was to look at -- to see if the -- if Triclosan increased the inflammatory response in tissue, right?
A. Yes.
Q. The ISO intracutaneous reactivity test in rabbits of Vypro mesh, Vypro Prolene composite, September 25, 2000 -- 2000, that was a -- that was a study that was -- well, do you know what the pore size of that Vypro Prolene composite was?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I could determine that by looking at the document, but I think it would be considered a large pore mesh.
BY MR. THORNBURGH:
Q. Larger pores than are contained within the Prolene TVT, correct?
A. Yes.
Q. The next study is an exploratory 91-day tissue reaction study -- let me make sure I got it right -- tissue reaction study in polypropylene-based surgical mesh in rats dated

Page 322

2001, right?
A. Yes.
Q. After that language was already contained in the IFU, right?
A. Yes.
Q. And, also, not a GLP study, was it?
A. That's correct.
Q. Not a good laboratory practices study, correct?
A. It should be differentiated from a FDA GLP study, which is in compliance with federal regulations.
All other non-GLP studies conducted at Ethicon are done in the spirit of GLP and are conducted in every manner like a GLP study, except for quality assurance unit oversight.
There's the -- following of the same SOPs, the same policies and procedures are applied, and the study is conducted as it would be under GLP other than quality assurance unit oversight.
Q. The next study you have listed there is a 28-day tissue reaction study of Prolene polypropylene mesh and autoclave Prolene polypropylene mesh implanted intramuscularly. We looked at that study yesterday. And that study,

Page 323

also a short-term study, showed up to a moderate inflammatory response, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. It was up to moderate with an average of mild.
BY MR. THORNBURGH:
Q. It was mild to moderate, correct? That was the summary in the study?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I recall it was -- we can check. I recall it was minimal to mild. Let me just look at that quickly.
Tab 36.
In that summary, then, the reaction was typical for implanted Prolene mesh and consisted of an initial mild to moderate subacute inflammation which gradually changed with time into a minimal to moderate chronic form body reaction.
BY MR. THORNBURGH:
Q. The histological evaluation in comparison to mechanical pullout strength of Prolene mesh and Prolene Soft mesh in a rabbit model. That's dated 2002, right?

Page 324

A. Yes.
Q. How many -- how many days or weeks was that study?
A. Let me confirm.
That would be Tab 37.
That study was out to 14 days. Implantation.
Q. So, clearly, a short-term study, correct?
A. Yes.
Q. You have a 90-day subchronic toxicity study after intraperitoneal implantation of a laminated composite composed of soft Prolene mesh PDS film and INTERCEED fabric.
That's not TVT mesh, is it?
A. No.
Q. A 24-week intramuscular study in rats comparing trilaminate prototype from Project Coyote of soft Prolene polypropylene mesh, that's clearly not TVT, is it?
A. That's just another variant of Prolene polypropylene mesh.
Q. It's not TVT, is it?
A. No.
Q. What is the pore size?

Page 325

A. This would be considered relatively large pore size.
Q. Larger than the pores in the TVT, correct?
A. Yes.
Q. A three-month preclinical trial to assess the fixation force of a new TVT-X and a sheep model. That was, I think, a 12-week study, right?
A. It says three months.
Tab Number 40.
Q. Yeah. It would be a short-term study, wouldn't it?
A. That would be considered a subchronic or mid-term study.
Q. Not a long-term study, correct?
A. That's correct.
Q. And the primary endpoint in that study was to look at the pullout force, correct?
A. Let me just take a look at 40. I think there were other endpoints.
Q. Right, but the primary endpoint was to look at the pullout force.
A. Well, I'll confirm in a moment.
Q. By the way, did you ever find the pathology report related to this study?

Page 326

MR. THOMAS: Object to the form of the question.
THE WITNESS: We're still looking for that.
BY MR. THORNBURGH:
Q. Did you inquire about the lost slides yesterday?
MR. THOMAS: Object to the form of the question.
THE WITNESS: No.
BY MR. THORNBURGH:
Q. Did you inquire with anybody whether or not --
A. Can I answer the question of a couple ago, and then we can move forward?
Q. Sure. I think my question was --
MR. THOMAS: Excuse me. He's looking for the primary endpoint.
MR. THORNBURGH: I am trying to refresh his memory.
MR. THOMAS: If he -- he's looking right now. If you want to ask him a different question --
MR. THORNBURGH: I was going to remind him that my question related to the primary

Page 327

endpoint of the study, Dave.
MR. THOMAS: Please, Dan. This is going to be a long day, and you're very contentious with the witness and with me this morning. I understand we didn't end on the best of terms yesterday. Excuse me --
MR. THORNBURGH: I am being at my best behavior right now.
MR. THOMAS: Well, please. Just slow down. Let the witness answer the question, and let him finish his answer before you ask another one. That's what he's doing right now.
THE WITNESS: The aim of this preclinical study was to evaluate less invasive TVT mesh, and then it goes on.
BY MR. THORNBURGH:
Q. Goes on to say what?
MR. THOMAS: He's going to tell you, Dan.
THE WITNESS: Studying the fixation phase divided into three components.
And then -- yeah. So I would conclude that the primary objective is biomechanical with a histology component included.
BY MR. THORNBURGH:

Page 328

Q. What steps did you take yesterday to locate the pathology report?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I did not take any steps.
BY MR. THORNBURGH:
Q. Did you make an inquiry to Joerg Holste whether or not any of the meshes that were explanted in that study showed encapsulation of the mesh?
A. No.
Q. Did you make an inquiry with anybody yesterday as to whether or not any of the slides were lost?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. During or -- during or after that study was conducted?
A. No.
Q. And in the next document you have listed here is an investigational study of Swine models to evaluate mesh contraction and tissue integration over a 13-week period.

Page 329

That would be considered a short-term study, correct?
A. That would be a mid-term study.
Q. Not a long-term study, right?
A. That's correct.
Q. How long does it take before mesh starts to contract?
MR. THOMAS: Object to the form of the question; scope.
BY MR. THORNBURGH:
Q. Are you prepared to answer that question today?
MR. THOMAS: Object to the form of the question.
THE WITNESS: No -- because it depends on a lot of factors. And if there are any specific studies you want to talk about that are in the compilation of documents that we've provided, I'd be glad to talk about those.
BY MR. THORNBURGH:
Q. Well, Ethicon studies showed that Prolene mesh can shrink up to 30 to 50 percent, right?
MR. THOMAS: Object to the form of the question; scope.

Page 330

Dan, that's not even on the designations --
BY MR. THORNBURGH:
Q. Are you prepared to discuss that today, Doctor?
A. No.
Q. Well, I mean, what is part of the designations is porosity studies. And that -- porosity studies, clearly, one of the things that you can look at is mesh contraction.
Did you look at any studies involving mesh contraction --
MR. THOMAS: Object.
BY MR. THORNBURGH:
Q. -- other than -- other than the one that you have listed here?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: This is one that we've conducted, Tab 41.
BY MR. THORNBURGH:
Q. What mesh was involved in that case?
A. I'll have to look at the detail.
Q. Let me just try to simplify. Was TVT mesh involved in that case?

Page 331

A. Let me confirm.
Q. Perhaps it was the heavyweight small pore.
MR. THOMAS: You've asked three questions. You haven't let him answer any of them yet. Let him answer a question, please.
THE WITNESS: Three mesh implants were studied: Prolene mesh, Prolene Soft mesh, and ULTRAPRO mesh.
Although it doesn't indicate the version of Prolene mesh, the date of the study, 6/21/07, would suggest that it's 5 mil flat mesh.
BY MR. THORNBURGH:
Q. Which is a different mil that is used -- different Prolene fiber size than is used in the TVT Prolene mesh, correct?
A. Yes.
Q. Do you know what the pore sizes are in that particular Prolene mesh that was studied?
MR. THOMAS: Object to form; asked and answered.
THE WITNESS: I know that it's less than the 6 mil TVT mesh.
BY MR. THORNBURGH:
Q. Does it say current production,

Page 332

Prolene mesh?
A. No, it does not.
Q. So you don't know sitting here today if that's the current production at the time or if that was some sort of prototype of the Prolene mesh, do you?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I think if it were a prototype, it would indicate such.
What I have in front of me is not sufficient to positively identify that was 5 mil mesh, but all the data points are in that direction.
BY MR. THORNBURGH:
Q. You can't tell from looking at that if it's a 3.5 mil Prolene mesh, can you?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes, I can.
BY MR. THORNBURGH:
Q. How can you tell?
A. Because that would be Prolene Soft mesh.
Q. And it doesn't indicate it's Prolene Soft. Is that what you're saying?

Page 333

A. No, it does indicate it is Prolene Soft. Prolene Soft is one of the meshes that were evaluated.
Q. What you can say for certain is that that mesh wasn't the Prolene mesh contained within TVT?
A. I can't say that for certain, but I believe it is not.
Q. You have the biocompatibility risk assessment report for Proceed's surgical mesh. Is that a large -- is that a lightweight large pore mesh?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. The Proceed?
A. This would be Prolene Soft mesh.
Q. So it's a 3.5 lightweight mesh, correct?
A. Yes.
Q. Not the same mesh in TVT, correct?
A. That's correct.
Q. Then you have the biocompatibility risk assessment report for the Gynecare TVT product family. That's -- that would be related to --

Page 334

that's the TVT product, right?
A. Yes.
Q. So you would agree with me that the vast majority of the documents that you listed in your list regarding the statement that Prolene mesh elicits a minimal inflammatory reaction in tissue which is transient, either were suture studies, not mesh studies, short-term studies, not long-term studies or mid term, not long-term studies, or involved -- some of the studies involved meshes that were large pore lightweight meshes, correct?
MR. THOMAS: Excuse me. Object to the form of the question.
THE WITNESS: All of those studies are included in this list.
BY MR. THORNBURGH:
Q. Did you ever conduct a study or did Ethicon ever conduct a study that looked at the TVT -- strike that.
Did Ethicon ever conduct a study that looked at the Prolene mesh in the TVT and compare it to a negative control to determine the inflammatory response in TVT?
A. No. That would not be so useful.
Q. You -- ULTRAPRO was compared to

Page 335

Prolene, wasn't it?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: In the study that I just mentioned, yes.
BY MR. THORNBURGH:
Q. Well, do you recall -- do you recall doing a study that looked at --
A. I just want to clarify which study that was, because we've been talking about a lot of studies.
That would be Tab 42.
Q. Can you read off the name of that study for me?
A. An investigational study of Swine models to evaluate mesh contraction and tissue in growth over a 13-week period.
I misspoke.
It's the same study, but the study that I intended to call out was Tab 41.
Tab 42 is simply the pathology report for that study.
Q. Do you recall doing a study that looked at the tissue response to ULTRAPRO and compared it to the old construction heavyweight

Page 336

Prolene and found that the tissue response was -- there's a greater inflammatory response with the old construction 6 mil Prolene compared to the ULTRAPRO?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I don't believe so.
BY MR. THORNBURGH:
Q. Do you know if that study was ever conducted?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I am not aware of such a study. It's not a study that we provided.
BY MR. THORNBURGH:
Q. Like we talked about yesterday when we talked about the porosity studies, was there a larger list that was created by you or someone else which contained more studies that are currently listed in this section regarding the studies related to the statement that the inflammatory response is minimal and transient?
MR. THOMAS: I'm sorry. Object to the form of the question. I'm trying to go with my screen and I've lost my --
(Brief interruption.)

Page 337

THE VIDEOGRAPHER: We're now going off the video record. It's now 9:45.
(Short break.)
(Whereupon, the court reporter read back the requested portion of the record.)
THE VIDEOGRAPHER: Back on the video record, 9:56.
THE WITNESS: Now, it's my understanding that the literature search results from the two literature searches conducted have been provided to the plaintiff's counsel. That includes all the studies in their entirety that came from that literature search of RDCS.
BY MR. THORNBURGH:
Q. Is that list larger than the list that you provided in Exhibit 2241?
MR. THOMAS: Those are the lists of the gross searches that were provided from 1960 to 1980 and then the two searches from 1980 to 2000. Those are the lists that we're talking about.
MR. THORNBURGH: I am asking the witness.
MR. THOMAS: That's fine.
THE WITNESS: Could you repeat?
BY MR. THORNBURGH:

Page 338

Q. Yes. Is there a larger list of studies than is contained in your section regarding the minimal and transient inflammatory response?
A. Yes, there is a larger list, as I've described.
From those two literature searches, studies were obtained from R&D central file, which were felt to be relevant to each of the topics under discussion.
Some of those studies turned out not to be relevant. Those studies that were determined to be relevant to each of the topics for discussion were then compiled for this particular topic. You see this list of 44 documents.
Q. Now, if there was a study that looked at and compared ULTRAPRO, which is a lightweight large pore mesh, to Prolene 6 mil mesh, that study did not make it onto your list, did it?
A. It would have fallen out of the original R&D central file search, and it would have been included in this list, because it would have contained TVT mesh, even though it's a comparison to some other mesh.
So that would have definitely been relevant.

Page 339

Q. You don't see any study on this list that you provided -- strike that.
You chose what documents -- what studies would be listed in your IFU list of studies that support the claim that the inflammatory response is minimal and transient, right?
A. Yes.
Q. And nowhere on that list is a study that compared ULTRAPRO to Prolene and found that ULTRAPRO elicited a more minimal inflammatory response, correct?
A. That is not on this list, and I am not aware of such a study.
Q. That would have been a relevant study to include on this list if it existed, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. That would have been a relevant study to do to compare the difference in inflammatory response of a lightweight large pore mesh to TVT, correct?
MR. THOMAS: Object to the form of the question.

Page 340

THE WITNESS: Yes, it would have been a relevant study.
BY MR. THORNBURGH:
Q. Of the 44 studies that made it onto your final list to support the claim that TVT elicits a minimal transitory inflammatory response, 31 of those studies are suture studies, correct?
A. I accept your count.
Q. Well, Tab 1 through Tab 31, correct?
A. I've not been keeping track.
Q. And of the 13 studies involving mesh --
A. Excuse me. Just for clarification, I was just scanning the 1 through 31, and I see that Number 10 is, in fact, a 1973 study with Prolene mesh. It's the same mesh.
Q. Oh, I'm sorry. Correct.
So of the first 31 studies, only one involved Prolene mesh, correct?
A. Yes.
Q. And that one study in the first 31 was a short-term study, correct?
A. Yes.
Q. And that's the study that formed the basis of the language in the IFU that the Prolene

Page 341

mesh in TVT would elicit a minimal transient inflammatory response, right?
A. That 1973 study needs to be considered in context with the NDAs for Prolene suture, where long-term studies were conducted two years in rat, three years in dog, three months in rabbits, looking at the same polypropylene -- Prolene polypropylene fiber that's used in Prolene mesh.
It's the leveraging of those long-term studies and the 1973 study, which is relatively short term as you point out, forms the basis for the information provided by preclinical to the folks that prepare the IFU.
MR. THORNBURGH: Move to strike; nonresponsive.
BY MR. THORNBURGH:
Q. In that list -- in fact, in this entire list of 43 studies, 44 studies, that is the only Prolene mesh study that formed the basis for the claim in the IFU that the Prolene and TVT will elicit a minimal transient inflammatory response, correct?
MR. THOMAS: Object to the form of the question; scope.

Page 342

THE WITNESS: I don't believe the results from the 1973 Prolene mesh study that went for 28 days can be assessed without considering the long-term results from the Prolene suture studies documented in the Prolene suture NDA.
MR. THORNBURGH: Move to strike; nonresponsive.
BY MR. THORNBURGH:
Q. Answer my question, please.
MR. THOMAS: He did answer your question.
BY MR. THORNBURGH:
Q. My question is: In this list of 43 studies -- 44 studies, the short-term 28-day study from 1973 was the only Prolene mesh study that formed the basis for the claim in the IFU that the Prolene in TVT will elicit a minimal transitory inflammatory response. Correct?
A. Yes.
Q. Of the 13 mesh studies contained within your IFU list of studies that support the claim that Prolene mesh in TVT elicits a minimal transient inflammatory response, approximately 12 of those were either short-term or mid-duration studies, correct?

Page 343

MR. THOMAS: Object to the form of the question.
THE WITNESS: I accept your count.
BY MR. THORNBURGH:
Q. You also have been designated as the person most knowledgeable regarding preclinical or animal studies that support the claim in the IFU that the material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes, correct?
A. That's correct.
MR. THOMAS: Object to the form of the question.
I think if you look at the topic that he was identified on, it was a single sentence. And that is the scope of the designation.
THE WITNESS: Well, I stand corrected. I have in front of me a compilation of studies that address a topic for discussion, and that topic indicates -- and I quote: The material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes. End quote.
BY MR. THORNBURGH:
Q. Which is the exact question I asked.

Page 344

MR. THOMAS: I don't think you did.
BY MR. THORNBURGH:
Q. Let me ask it again. I'll read from the transcript.
You also have been designated as the person most knowledgeable regarding preclinical or animal studies that support the claim in the IFU that the material is not absorbed, nor is it subject to degradation or weakening by action of tissue enzymes.
Correct?
MR. THOMAS: Object to the form of the question. That's not the designation.
The designation is and it reads verbatim in terms that you've written: The identity of, the location of, and the substance of any and all studies, data, and/or evidence that form the basis of the following claim/statement contained in the attached instructions for use for the TVT products. Animal studies show that implementation of Prolene mesh elicits a minimal inflammatory -- I'm sorry.
MR. THORNBURGH: You're looking at the wrong designation.
MR. THOMAS: Okay. I am. Let me

Page 345

start over again. I have the right one now.
The designation made by plaintiffs states, Paragraph 3: The identity of, the location of, and the substance of any and all studies, data, and/or other evidence that form the basis of the following claim/statement included in the attached instructions for use for the TVT products. The material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes.
That's the designation.
BY MR. THORNBURGH:
Q. So you've been designated as the person most knowledgeable regarding studies or evidence that support the claim in the IFU that the Prolene mesh in TVT is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes. Correct?
A. Yes.
Q. In other words, the claim by Ethicon in the IFU is that the Prolene mesh in the TVT will not degrade, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: It says that it's not

Page 346

absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes.
BY MR. THORNBURGH:
Q. Is it Ethicon's position that the studies and evidence support the claim that the Prolene mesh in TVT will not degrade?
MR. THOMAS: Object to the form of the question.
THE WITNESS: In a general sense.
BY MR. THORNBURGH:
Q. What do you mean by "in a general sense"?
A. Well, that statement is different from the statement that's in the IFU.
Q. Part of the statement is that the Prolene mesh in the TVT will not degrade, right, by the tissue enzymes in the human body. Correct?
A. Yes.
Q. Is that Ethicon's position?
A. Yes.
Q. Is it Ethicon's position that the Prolene in the TVT is subject to degradation under certain conditions?
MR. THOMAS: Object to the form of the question.

Page 347

THE WITNESS: That's not what this says.
BY MR. THORNBURGH:
Q. Well, is it Ethicon's position that the Prolene mesh will degrade under certain -- in certain environments?
MR. THOMAS: Object to the form of the question.
THE WITNESS: It's Ethicon's position, as outlined in these two folders that contain 49 different studies, that the material in TVT mesh, which is Prolene polypropylene, is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes.
BY MR. THORNBURGH:
Q. Now, you agree with me that Ethicon has conducted studies which have shown that in vivo, in the human body, or in animal studies, the Prolene mesh does, in fact, suffer from surface cracking on the outer layer of the mesh?
MR. THOMAS: Object to the form of the question.
THE WITNESS: You're making reference to surface changes observed in a seven-year dog study?

Page 348

BY MR. THORNBURGH:
Q. No, there's more than that, but we'll talk about the dog study.
But you agree that there have been studies conducted at Ethicon that show degradation of the surface layer of the Prolene mesh?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I only know of one study looking at surface changes in Prolene suture. That would be the seven-year dog study.
And that would be -- that would be Tab 33, seven-year data for ten-year Prolene study. ERF 85-219 1992.
BY MR. THORNBURGH:
Q. Did you look at the five-year data?
A. Yes, as part -- well, the five-year endpoints were part of this study.
MR. THOMAS: Just for the record, that tab has been supplemented by this additional disclosure. I'll make sure the witness has that available to him.
THE WITNESS: If we need to talk about the seven-year dog study, this would be the one to -- to discuss.

Page 349

MR. THOMAS: Excuse me. I need to take a very quick break.
THE VIDEOGRAPHER: 10:16, off the video record.
(Short break.)
THE VIDEOGRAPHER: Back on the video record, 10:20.
BY MR. THORNBURGH:
Q. Doctor, you would agree that the human body, due to the presence of O2 in various forms, is a potentially powerful oxidizer?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: They can't be too -- I would agree in general, but they can't be too powerful, because too powerful would be incompatible with life.
BY MR. THORNBURGH:
Q. Powerful enough to degrade polypropylene, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That would need to be determined.
BY MR. THORNBURGH:

Page 350

Q. Well, let me look at a document I believe you had listed on your list of evidence.
MR. THORNBURGH: We'll mark it as Exhibit 2250. ETH.MESH.10575391.
(Document marked for identification as Exhibit T-2250.)
BY MR. THORNBURGH:
Q. This is Critical Reviews in Biocompatibility. You've seen this?
A. Yes.
Q. Before, right?
A. Yes.
Q. It appears that the authors of this document is -- C.C. Chu?
A. Yes.
Q. And the referee is Postlethwait. Am I pronouncing his name correctly?
A. I am not certain. I don't know him. That sounds good to me.
Q. Do you know Dr. Chu?
A. I've met him once.
Q. Okay. And the title of this document is the degradation of biocompatibility -- I'm sorry. Strike that.
The degradation of -- strike that.

Page 351

The title of this, what appears to be a book or a chapter in a book, is the degradation of -- "The Degradation And Biocompatibility Of Suture Material," right?

A. Yes.

Q. Where does this come from? What's the critical reviews and biocompatibility; do you know?

A. Well, I've seen critical reviews in toxicology before. I think this is an attempt by CRC press to put forward review articles by experts, considered experts in the field, that would summarize what is known about a particular topic up to a certain point in time.

Q. And this is 1985, right?

A. Yes.

Q. This is before the TVT was marketed, correct?

A. Yes.

Q. In fact, it's before the TVT was designed and developed, correct?

A. Yes.

Q. Do you find this to be authoritative?

A. Up to 1985, yes. I think it reflects what was generally known to be so in the field.

Page 352

Q. And this document was -- if you look, there's an ETH.MESH. number on it, which would indicate that this document was within the files at Ethicon, correct?

A. Yes. I believe it's in -- here as Tab 22 in the IFU three-folder.

MR. THOMAS: Object to the form of the question.

BY MR. THORNBURGH:

Q. How did you find this document which made it to your list of supporting evidence regarding the claim in the IFU that the Prolene TVT does not degrade by the actions of enzymes in the human body?

A. It was one of the references that FDA provided when they reclassified Prolene polypropylene suture from Class 3 to Class 2.

And I think I -- yes. And that would be Tab 28 in the folder, IFU 3, entitled "FDA Reclassification Of Prolene Polypropylene Non-Absorbable Sutures, October 12, 1990."

Q. Now, the authors -- turn with me to Page 288 of the critical reviews.

The ETH.MESH. number is 10575419.

The authors are -- you've had a chance to review this before today, right?

A. I've read through this document at one point.

Q. The authors here in this paragraph are talking about polypropylene, right?

MR. THOMAS: Which paragraph are you talking about?

MR. THORNBURGH: I'm sorry. The third paragraph on Page 288, Bates number ending in 5419.

THE WITNESS: They're talking about polyethylene sutures of which polypropylene is one.

BY MR. THORNBURGH:

Q. Okay. And in the highlighted section, the authors write: Although this class of polymer is resistant to hydrolysis, it is susceptible to oxidative degradation. Oxidation is not as well known as hydrolysis in biomedical polymers in 1985. The human body, due to the presence of O2 in various forms, is a potentially powerful oxidizer.

Liebert and others examine the rate of oxidation of polypropylene fibers with and without antioxidants implanted subcutaneously in hamsters. They found that the pure fiber without

Page 354

antioxidants degraded by an oxidative mechanism similar to high temperature autooxidation.

The degradation began to occur after only about ten days, and this initiation period lasted about 108 days.

The degradation product -- do you know what that -- what that means right here, C equals O?

A. It is a carbonyl group.

Q. So: The degradation product, the carbonyl group, was observed in the form after 99 days of implantation. Whether this observation is applicable to polypropylene suture material is not known and needs to be further studied.

Do you see that?

A. Yes.

Q. How many studies are you aware of that Ethicon did to determine if the Prolene in TVT can degrade as a result of or including as a result of oxidation in vivo inside the body?

A. There are roughly -- well, there are -- there are 49 documents in these two -- two binders labeled IFU 3 that support the statement that's the subject matter topic that the material is not absorbed, nor is it subject to degradation or

Page 355

weakening by the action of tissue enzymes.
Q. How many preclinical studies were done that looked at the primary endpoint degradation of the Prolene fiber in TVT?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Every study where TVT was implanted, there is an opportunity to assess whether or not there's any degradation of the filaments and any resulting effects from that.
BY MR. THORNBURGH:
Q. What types of -- what types of tests are performed to determine degradation of polymer filaments?
A. The key endpoints to make a determination as to whether or not a material fiber would be degraded would be to look at quantitative parameters, like molecular weight and, perhaps most importantly, tensile strength.
In the absence of loss of molecular weight and in the absence of a loss in tensile strength, one cannot conclude that there's been any impact or degradation on a fiber.
Q. Do you know what I mean by when I say amorphous zones or amorphous regions of the Prolene

Page 356

fiber?
A. I have a general understanding.
Q. What is your understanding of amorphous zones or amorphous regions of the Prolene fiber?
MR. THOMAS: Object to the form; scope.
THE WITNESS: They're not crystalline, and they do not offer much contribution in the way of tensile strength.
BY MR. THORNBURGH:
Q. They're less stable than the crystalline bulk Prolene, correct?
MR. THOMAS: Object to form; scope.
THE WITNESS: They're different areas of the polymer.
BY MR. THORNBURGH:
Q. Less stable areas of the polymer?
MR. THOMAS: Excuse me. Do you want him to answer your question?
THE WITNESS: I don't know that I would characterize it as less stable. That might be a question for a polymer chemist. But, clearly, there are differences in mechanical characteristics between amorphous and crystalline regions, the

Page 357

crystalline regions offering the most strength of a fiber compared to the amorphous regions.
BY MR. THORNBURGH:
Q. One way of looking for degradation of Prolene would be through FTIR analysis, correct?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: That could be a way, and, more likely, IR microspectroscopy, where there is a very specific focus on areas of interest.
But, again, that's an analytical chemistry kind of area. Although I have some understanding of it, depending on how much detail you would need, I may or may not be able to help.
BY MR. THORNBURGH:
Q. And you're not at least prepared today to talk about carbonyl bands that show up on FTIR microscopy which would indicate oxidation of the Prolene fibers, correct?
A. That's right. I do not have enough depth in that area.
Q. Another way of analyzing degradation of a polypropylene like Prolene would be to look at melting point, right?
A. Again, that's -- that's a polymer

Page 358

chemistry kind of term, and I'm not prepared to address any melting point endpoints.
Q. Do you know -- do you know generally what I mean by melting point?
MR. THOMAS: Object to the form of the question.
THE WITNESS: It's the point -- it's the temperature at which a substance melts.
BY MR. THORNBURGH:
Q. Did you look at any -- before you came in today, did you look at any studies that were conducted by Ethicon that looked at the melting point of pieces of the outer surface of Prolene mesh which, when the study was conducted, showed evidence of oxidation of the polypropylene?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I've not reviewed any melting point data.
BY MR. THORNBURGH:
Q. And in any event, these authors write that the human body is potentially a powerful oxidizer, right?
A. It's as it's stated.
Q. And there's a discussion about a

Page 359

study by Liebert. Did you read the Liebert study before you came here today?
A. I am looking for it right now. Give me a moment to go through this list.
I don't see it in this list, but I have reviewed that publication.
Q. And you're familiar, then, in the Liebert study that when Liebert and his fellow investigators examined the rate of oxidation of polypropylene fibers, they found degradation in animal study -- in animal studies of the polypropylene fibers which did not contain antioxidants, correct?
A. That's correct, as reflected by C.C. Chu in this review article, when he says they found that the pure fiber (without antioxidant) degraded by an oxidation mechanism similar to high temperature autooxidation.
What he doesn't say here and what is called out in the Liebert paper is that the fiber with antioxidant did not show any evidence of degradation.
Q. Right. And one of the topics that you've been designated to discuss is leaching, right?

Page 360

A. Yes.
Q. And some of the studies that you looked at showed that the antioxidants, Santonox R and Lubrol, can leach out of the Prolene fiber, correct?
A. Let me take a look at the...
Q. You don't recall that off the top of your head?
A. I'd rather pull the folder and be able to give you a more complete answer.
This is a folder that contains --
MR. THOMAS: There are three of them.
BY MR. THORNBURGH:
Q. Let me ask you this question real quick.
A. Let me finish your other.
Q. Well, I'm going to withdraw the original question. I'm going to try to streamline these.
Is it Ethicon's position that the antioxidants in the polypropylene Prolene fibers in TVT can leach from the fibers?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes.

Page 361

BY MR. THORNBURGH:
Q. And could you explain to the ladies and gentlemen of the jury what we mean by "leach"?
A. Leaching means the movement of substances from an implant into the surrounding tissue.
Q. Okay.
MR. THOMAS: While you're doing this, are you going to ask him questions about the leaching notebooks?
MR. THORNBURGH: Not yet. We will be asking questions about leaching.
MR. THOMAS: We'll put them away, then.
BY MR. THORNBURGH:
Q. You've seen the Sunoco material safety data sheet previously, haven't you?
MR. THOMAS: Object to the form of the question.
I think this was covered at length in his prior deposition.
THE WITNESS: I think you showed this to me at the last deposition.
BY MR. THORNBURGH:
Q. Right. And this has been premarked

Page 362

as Exhibit Number T-2111.
Now, if you turn with me to --
Well, do you have an understanding that this is the same Prolene homopolymer as contained within the TVT Prolene?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Yeah. It's not the original supplier, but those suppliers may have changed. It may be the current supplier. I don't know that for certain, but if you -- if you say that this -- this is the source of the polypropylene resin for polypropylene-based products, I would not disagree.
BY MR. THORNBURGH:
Q. And Sunoco is a petro oil company, correct? Are you familiar with that?
A. Yes. Yes. It's Sun Oil company.
Q. If you turn with me to the fourth page, which is ETH.MESH.02026594, you would agree with me that this MSDS for polypropylene resin shows that -- under the incompatibility, that the following materials are incompatible with the product: Strong oxidizers, such as chlorine, peroxide, chromates, nitric acid, perchlorates,

Page 363

concentrated oxygen, sodium hypochlorite, calcium hypochlorite, and chlorine and nitric acid, correct?
A. Yes.
MR. THOMAS: You left out permanganates.
BY MR. THORNBURGH:
Q. Permanganates, chlorine, and nitric acid, correct?
A. Yes. That's the list.
Q. And you would agree with me that according to the evidence that you reviewed in preparing for this 30(b)(6) deposition, that the human body, as a result of the inflammatory response to foreign objects or foreign materials, can create strong oxidizers in the body?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Strong is a relative term. But I believe that the strong oxidizers as called out in this MSDS, that would make -- that would be incompatible with polypropylene would not be biocompatible in the body.
BY MR. THORNBURGH:
Q. Well, according to Exhibit Number 2250, which you listed on your list of

Page 364

evidence supporting your claims, the authors wrote that the human body, due to the presence of O2 in various forms, is a potential powerful oxidizer. Correct?
A. Again, in my opinion, they're not as strong chemically as these oxidizers called out in this MSDS that would not be compatible with polypropylene fiber or polypropylene material.
These oxidizers are not biocompatible. They are corrosive. They would not be compatible with tissue.
Q. Well, have you ever personally studied -- have you personally studied -- strike that.
Have you -- on behalf of Ethicon, did you do any in vivo animal studies to look at, as a primary endpoint, degradation?
MR. THOMAS: Object to the form of the question; scope.
BY MR. THORNBURGH:
Q. Do you know sitting here right now whether or not you ever did such a study?
MR. THOMAS: Which question do you want him to ask --
THE WITNESS: Well, I'll answer the

Page 365

one before that.
That answer is yes. There are two folders --
MR. THOMAS: Excuse me. Let him answer the question.
BY MR. THORNBURGH:
Q. My question was: Did you personally --
A. No. Your question was on behalf of Ethicon.
Q. Did you personally?
MR. THOMAS: Okay. Stop. Let's start over. And you ask a question that he can answer. You have five pending.
BY MR. THORNBURGH:
Q. Did you personally conduct any studies that had the primary endpoint of looking at degradation in animal studies?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Well, I understood I was here to talk on behalf of Ethicon and not myself personally.
MR. THOMAS: You can answer the question. Did you personally do that?

Page 366

THE VIDEOGRAPHER: It's 10:44. We're going off the video record.
This concludes Volume 2, Tape 1 of the videotape deposition of Dr. Thomas A. Barbolt.
(Short break.)
THE VIDEOGRAPHER: We're now back on the video record. It's 10:52.
This begins Volume 2, Tape 2 of the videotape deposition of Dr. Thomas A. Barbolt.
MR. THOMAS: There was a question pending. Do you want him to answer it?
MR. THORNBURGH: I thought he did answer it.
BY MR. THORNBURGH:
Q. Were you not finished answering my question?
A. I don't think so. Could you repeat? It's not on the...
MR. THOMAS: I don't think he answered it.
The question appears at Line 63, 23.
BY MR. THORNBURGH:
Q. Did you personally conduct any studies that had the primary endpoint of looking at degradation in your animal studies?

Page 367

MR. THOMAS: Object to the form of the question.
THE WITNESS: All implantation studies that I have conducted -- and you have seen my name on a number of them in the compilation of data that we provided looking at degradation of the implant -- is part of every implantation study. So the answer is yes.
BY MR. THORNBURGH:
Q. Did you do SEM EDX analysis?
A. No.
Q. Did you do FTIR analysis?
A. Is this on behalf of Ethicon or personally?
Q. Did you personally?
A. No.
Q. Did you do melting point analysis?
MR. THOMAS: Object to the form of the question.
THE WITNESS: No.
BY MR. THORNBURGH:
Q. So, clearly, the primary endpoint in the studies that you conducted were not oxidation or degradation studies, correct?
MR. THOMAS: Object to the form of

Page 368

the question.
THE WITNESS: They were not oxidation studies, but they definitely were degradation studies. That is a primary endpoint for any implantation study of absorbable or non-absorbable implants.
BY MR. THORNBURGH:
Q. Did you do SEM analysis?
MR. THOMAS: Object to the form of the question.
THE WITNESS: No.
BY MR. THORNBURGH:
Q. How could you do a degradation study without doing SEM analysis?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Well, the beauty -- the beauty of an implantation study is that you can look at the elements of an implant to determine whether or not there is cracking, there's absorption, there is surface effects. All that could be visualized directly under the light microscope.
BY MR. THORNBURGH:
Q. In fact, you were told not to do degradation studies, weren't you?

Page 369

MR. THOMAS: Object to the form of the question.
THE WITNESS: I don't understand the question. In what context?
BY MR. THORNBURGH:
Q. Do you recall being told -- do you -- strike that.
Do you recall inquiring about whether you should conduct animal studies with the primary endpoint of degradation?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Being told not to do such studies?
BY MR. THORNBURGH:
Q. Yes.
A. No.
Q. Do you know who Dr. Ramshaw is?
A. Dr.?
Q. Ramshaw?
A. No, I do not.
Q. Bruce Ramshaw from the University of Missouri?
A. I don't think we've met.
Q. My question was: Do you know of him?

Page 370

A. No.
Q. I've handed what's been premarked as Exhibit Number T-4012.
The ETH.MESH. number is 05588123.
Now, if you go to the last page of this e-mail, which would be the first e-mail in this e-mail string, you write to Dr. Thomas Divilio.
Do you know who Dr. Thomas Divilio is?
A. Thomas Divilio.
Q. Divilio? Who's Dr. Thomas Divilio?
A. He was a medical director at Ethicon.
It doesn't look like I sent the message. It looks like I was copied on it.
MR. THOMAS: He directed your attention to the very end.
Oh, I see. Yes, I see what you mean.
THE WITNESS: I am looking at the last e-mail message beginning on ETH.MESH.05588125.
BY MR. THORNBURGH:
Q. Yeah. Oddly, if you look at the author of this e-mail, it appears to be you.
Hold on a second.
MR. THOMAS: Wait a minute.
MR. THORNBURGH: I'm sorry. Sorry.

Page 371

Strike that. Strike that.
MR. THOMAS: The author is Tom Divilio.
MR. THORNBURGH: That's why I said "strike that".
BY MR. THORNBURGH:
Q. Well, let's do it this way. Do you recall being included in an e-mail, copied in an e-mail, from Dr. Thomas Divilio to John Gillespie where you were copied --
MR. THOMAS: Object to form.
BY MR. THORNBURGH:
Q. -- as a recipient of the e-mail?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Well, I've never seen this e-mail chain before. I'd like to take a minute to go -- to read through it.
BY MR. THORNBURGH:
Q. Well, you clearly received it. You don't recall it. Is that what you're saying?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I see that I'm copied on it. You asked me if I knew anything about it.

Page 372

BY MR. THORNBURGH:
Q. We'll read the e-mail.
It says from Dr. Divilio, John --
MR. THOMAS: I think he wants to read the whole chain.
MR. THORNBURGH: Okay. I mean, I am going to read it with him.
THE WITNESS: Okay. If you want to lead it off, that's fine.
BY MR. THORNBURGH:
Q. It says: John, Bruce Ramshaw from the University of Missouri is challenging our perception of polypropylene --
Polypropylene is the polymer in TVT, correct?
A. Yes.
Q. -- is challenging our perception of polypropylene as inert material after implantation. In a recent article, his group looked at explanted polypropylene from a Bard Composix mesh under EM and found that the surface of the fibers had been altered with respect to the pristine material, with evidence of blistering and increased surface roughness, possibly due to oxidation. We previously had implanted Prolene suture into dogs, and explants

Page 373

after ten years revealed no changes in material.
That's not actually true, is it?
MR. THOMAS: Object to the form of the question; scope.
BY MR. THORNBURGH:
Q. That statement that Ethicon had previously implanted Prolene suture into dogs, and explants after ten years revealed no changes in the material, is not a true statement, is it?
MR. THOMAS: Object to form; scope.
THE WITNESS: There were three elements, three important elements in that study.
The key elements, as we've discussed earlier, were molecular weight and tensile strength. And in that seven-year dog study, which -- which is referenced as ten year here, there was no impact on molecular weight, nor tensile strength.
BY MR. THORNBURGH:
Q. There was surface cracks observed on the surface layer of the polypropylene in that study, correct?
A. Surface changes were observed in some of the fibers in some of the dogs.
Q. Are you telling the ladies and gentlemen of the jury that when the outer surface of

Page 374

the polypropylene fibers crack and peel away from the surface, that that is not degradation?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I am telling listeners that the key endpoint of adverse effects of degradation are molecular weight and tensile strength, both quantitative measures, not subjective assessments of surface changes, but quantitative measures that hold great weight and suggest that there's no degradation to the Prolene fiber in terms that are significant.
BY MR. THORNBURGH:
Q. Do you agree there's been studies conducted that show that when the polypropylene fiber surface or lose -- or fragments come off of the polypropylene surface as a result of degradation, that that increases the inflammatory response?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. You've seen those studies, haven't you?
MR. THOMAS: Object to the form of

Page 375

the question.
THE WITNESS: I don't recall those studies. However, all of those studies I do recall -- and it's those 49 studies listed in these two folders -- do not suggest that there's degradation of the Prolene polypropylene fiber.
BY MR. THORNBURGH:
Q. Do you agree on behalf of Ethicon that if that -- that if the surface layer is coming off and/or there are fragments that are being released from the polypropylene, that that would -- could increase -- increase the inflammatory response?
A. No.
MR. THOMAS: Object to the form of the question.
THE WITNESS: No, because every bit of data that Ethicon has -- and there are 49 studies listed here -- suggest that if anything, the tissue reaction after long-term implantation of Prolene polypropylene fibers diminishes. It does not increase.
And this is reflected by FDA in the FDA reclassification document, where they discuss what's known about Prolene suture and that, in fact,

Page 376

that it's not absorbable and doesn't degrade to a significant effect.
MR. THORNBURGH: Move to strike.
BY MR. THORNBURGH:
Q. It's a yes or no question, and then you can explain it if you want to.
My question to you was: Is it Ethicon's position --
MR. THOMAS: Excuse me. Just so you know, he said "no" and then explained. That's exactly what he did.
MR. THORNBURGH: All right. Move to strike everything after no.
It's going to be a long day if -- counsel --
BY MR. THORNBURGH:
Q. Counsel, obviously, is going to have an opportunity to ask you questions. But I asked a yes or no question. I expect a yes or no answer.
MR. THOMAS: He knows the rules, Dan. This is his sixth day.
BY MR. THORNBURGH:
Q. Doctor, in fact, one of the pieces of evidence that you included in your list of documents related to the statement by Ethicon that the Prolene

Page 377

in TVT does not degrade as a result of tissue enzymes is a study conducted by Postlethwait, right?
You recall this study, don't you?
MR. THOMAS: Which one are we talking about?
BY MR. THORNBURGH:
Q. Long-term comparative study of non-absorbable sutures by Dr. Postlethwait from 1969. ETH.MESH. Number 10575759.
MR. THOMAS: Excuse me. Do you want to mark one of those for the record?
MR. THORNBURGH: Yes. Yes, I do.
THE WITNESS: Did you say 59?
MR. THOMAS: Wait a minute. He's going to mark it for you.
MR. THORNBURGH: I am going to give you a copy so you have it.
THE WITNESS: I have a copy here. It's Tab --
MR. THORNBURGH: I am going to mark this one, anyway.
I'm sorry, Dave.
MR. THOMAS: Can I have one, please?
MR. THORNBURGH: Yep.
MR. THOMAS: What exhibit number is

Page 378

that?
THE WITNESS: 2251.
MR. THOMAS: 2251. Thank you.
(Document marked for identification as Exhibit T-2251.)
BY MR. THORNBURGH:
Q. Now, Dr. Postlethwait from Duke University Medical Center in 1969, in a study supported by Ethicon, looked at degradation of polypropylene fibers or sutures.
And if you turn to Page 895, and if you go to the -- first figure six at the bottom, it shows that M -- this is a hard copy to read, but in Picture M or Image M, polypropylene -- apparently, Image M is showing polypropylene with some fragments after 18 months.
Same at two years. Higher power of edges of polypropylene suture and fragments.
Now, if we turn to ETH.MESH.0175763, the last full paragraph on the left-hand column discusses Dr. Postlethwait's findings with respect to the polypropylene sutures which were apparently provided to him by Ethicon.
MR. THOMAS: Whoa, whoa, whoa. Object to the form of the question. Where can you

Page 379

substantiate that?
MR. THORNBURGH: Well, it's provided in part by Ethicon.
MR. THOMAS: Nowhere in this article does it say these are Ethicon sutures, unless you can show me otherwise.
MR. THORNBURGH: Are you representing that they're not?
MR. THOMAS: I am not, but I think it's another thing to say that they were.
BY MR. THORNBURGH:
Q. Well, certainly, Ethicon is supporting this study, right?
And this study is regarding polypropylene degradation. And Dr. Postlethwait writes that in 18 months and more -- at 18 months, and even more often at two years, an occasional suture has started to fragment. The entire suture does not break up, but small portions appear to separate from one edge.
Each minute fragment, although remaining in the vicinity, stimulates its own cellular reaction. This, of course, increases the grade of the tissue reaction so that it exceeds nylon.

Page 380

So Dr. Postlethwait, who personally studied this issue with polypropylene, found that fragments, no matter how minute, increases the grade of tissue reaction.
Do you disagree with Dr. Postlethwait's statement here?
MR. THOMAS: Object to the form of the question.
THE WITNESS: He says: This, of course, increases the grade of the tissue reaction so that it exceeds nylon.
BY MR. THORNBURGH:
Q. It increases the tissue reaction, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: To exceed nylon, which I know has virtually little reaction.
BY MR. THORNBURGH:
Q. It increases the tissue reaction, correct?
A. Yes.
Q. You would agree with that statement, wouldn't you?
A. Yes.

Page 381

MR. THOMAS: He already has.
BY MR. THORNBURGH:
Q. Now, if we go back to Exhibit Number 4012: Bruce, the e-mail from Dr. Divilio to John Gillespie.
Who's John Gillespie?
A. He worked in the Gynecare group, so...
Q. And you were cc'd, weren't you?
A. Yes.
Q. And the subject of this e-mail is how inert is polypropylene, right?
A. Yes.
Q. Okay. Now, Dr. Divilio writes to John: Bruce Ramshaw from the University of Missouri is challenging our perception of polypropylene as an inert material after implantation.
Do you recall other experts in the field who have evaluated and studied the potentiation of polypropylene degradation having a different position than Ethicon has currently in this litigation?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yeah. You'll have

Page 382

to -- are we talking about this memo, or is it a standalone question?
BY MR. THORNBURGH:
Q. Standalone question first.
A. And that would be?
Q. Experts in the field who study degradation of polypropylene have a different position than Ethicon is taking through you in this litigation, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: The position that Ethicon is taking, there's no impact on molecular weight or tensile strength. I don't know of other investigators that demonstrate with Prolene polypropylene fiber a loss of molecular weight and loss in tensile strength.
BY MR. THORNBURGH:
Q. Are you saying Ethicon that is not taking the position that the surface layer of the polypropylene fibers does, in fact, crack and can peel away from the surface of the fibers?
MR. THOMAS: Object to the form of the question.
THE WITNESS: We can look at the

Page 383

details of the seven-year dog study which do show surface changes in some of the fibers from some of the dogs.
MR. THOMAS: Excuse me --
THE WITNESS: In the absence --
MR. THORNBURGH: I thought he was done, Dave.
THE WITNESS: In the absence of impact of molecular weight or tensile strength.
BY MR. THORNBURGH:
Q. Right. But you agree Ethicon -- as a spokesperson for Ethicon, that the surface of the polymer fibers can, in fact, crack and peel away into the surrounding tissue of either the patient or an animal?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I recall observations of surface cracking in the seven-year dog study, but I don't recall any discussion of surface peeling away and -- to your -- to your detail.
BY MR. THORNBURGH:
Q. Well, we'll look -- we'll look at some other studies here in a moment. But let me at least understand Ethicon's position with respect to

Page 384

surface cracking.
Is it Ethicon's position that the polymer fiber surface can, in fact, crack?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Such observations were made in the seven-year dog study.
BY MR. THORNBURGH:
Q. So it's Ethicon's position that the polymer fibers can crack, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Again, the seven-year dog study talks about surface changes. The etiology of those changes or their significance are not discussed in detail other than to follow up on that observation and look at more important quantitative parameters, like molecular weight and tensile strength, and those two parameters were not adversely affected.
BY MR. THORNBURGH:
Q. I know you want to try to frame the position most favorable to Ethicon, but listen to my question. Okay?
MR. THOMAS: Please don't load the

Page 385

question.
BY MR. THORNBURGH:
Q. Do you agree as a spokesperson for Ethicon that the polymer fibers can crack?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I think I just answered that --
BY MR. THORNBURGH:
Q. Yes or no?
A. I think I just answered that those observations are in the seven-year dog study. So we can look at those details if you care to.
Q. So you would agree as a spokesperson -- as a 30(b)(6) person for Ethicon that the surface of polymer fibers, including the polypropylene fibers in TVT, can crack?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. And you would agree that if fragments come off of the polypropylene fibers, including the polypropylene fibers in TVT, that that could increase or that could cause each minute fragment to

Page 386

stimulate its own cellular reaction. You would agree with that, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: No. There's no evidence that there's -- in the seven-year dog study that material that is coming from the surface other than showing surface changes in the form of -- of cracking.
I should add that in the Prolene suture NDA, observations of polypropylene fragments were observed and reported to the FDA. And they were felt to be related to this swaging process or the cutting of suture strands to length, and a fragment would be attached to the suture and get inadvertently implanted.
I should also point out in the Postlethwait study that we just discussed, Exhibit 2251, ETH.MESH.10575764, at the top of the page, right after the discussion section where it says that there are fragments which increase the tissue reaction -- at the top of the page, it says:
In correspondence with the manufacturer, it was learned that these sutures were the first extruded from the first shipment of

Page 387

polypropylene. Subsequently, changes have been made to improve the extrusion process. It is believed that fragmentation will not occur with the presently available sutures. Additional long-term studies have been initiated, however.

And then, parenthetically, the polypropylene did retain tensile strength.

BY MR. THORNBURGH:

Q. It still increased the inflammatory response, didn't they?

MR. THOMAS: Object to the form of the question.

THE WITNESS: An individual fragment adjacent to a strand of polypropylene -- Prolene polypropylene fiber will add to the inflammatory reaction just like there is an inflammatory reaction to the suture fiber itself.

That's wholly different than what you're talking about when you suggest that there's surface cracking and sloughing of the surface, releasing many particles.

If that's the case, that observation would have been observed -- that observation of increased tissue reaction would have been observed in the 49 studies that we've compiled to demonstrate

Page 388

that, in fact, that that does not occur; and, in fact, there's a diminution of the tissue reaction over time in many cases from Ethicon's data and as called out by FDA in the reclassification.

MR. THORNBURGH: Move to strike.

BY MR. THORNBURGH:

Q. We're going to be here a long day if you keep on going on this platform and speaking when there's not even a question pending.

MR. THOMAS: Please don't lecture the witness.

MR. THORNBURGH: Move to strike.

MR. THOMAS: Please don't lecture the witness.

BY MR. THORNBURGH:

Q. Dr. Barbolt, where in this section in the IFU that talks about degradation does Ethicon warn physicians that the surface layer of the Prolene in the TVT mesh can crack?

MR. THOMAS: Object to the form of the question; scope.

BY MR. THORNBURGH:

Q. It's not in there, is it?

A. This is an IFU intended to provide the most useful information to surgeons who use our

Page 389

products.

Q. Don't you think surgeons should know that the -- that the surface layer of the TVT mesh, a device that's being implanted permanently in women's pelvises -- don't you think they should know and be made aware that, in fact, the tissue enzymes can cause the surface layer of the TVT to crack?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: To the first part of your question, no, I don't think they care...if, there's no impact on molecular weight and there's no increase -- there's no decrease in tensile strength. And all the tissue reaction studies show a very minimal tissue reaction and, in fact, a diminution of that reaction over time.

BY MR. THORNBURGH:

Q. You don't think physicians should be made aware of the potential of degradation of the -- or surface cracking of the polymer fibers that's being used as a permanent implant in women's pelvises? That's what you're telling the ladies and gentlemen of this jury?

MR. THOMAS: Excuse me. Object to the form of the question; scope.

Page 390

THE WITNESS: Could you repeat the question?

BY MR. THORNBURGH:

Q. Yeah. Let me say it this way.

Ethicon chose not to include information in this section from animal studies that showed that the -- that the Prolene and polypropylene surface area can crack, right?

MR. THOMAS: Object to the form of the question.

THE WITNESS: I believe that Ethicon did not feel that that was important information to put in the instructions for use.

BY MR. THORNBURGH:

Q. And because that information wasn't put into the -- and because Ethicon chose not to put that information in the IFU, that information, therefore, did not make it to the physicians?

MR. THOMAS: Object to the form of the question; scope.

BY MR. THORNBURGH:

Q. Correct?

A. That level of detail was not provided in the package insert.

MR. THORNBURGH: I have to use the

Page 391

restroom.
THE VIDEOGRAPHER: Off the video record. The time is 11:18.
(Short break.)
THE VIDEOGRAPHER: Back on the video record. It's 11:24.
BY MR. THORNBURGH:
Q. Now, Doctor, you made a statement a moment ago regarding the Postlethwait publication study, that changes were made by the manufacturers subsequent to this study, correct?
A. Yes, as I read from the publication.
Q. And this study was 1969, right?
A. Yes. A Prolene suture was just being released as a new product.
Q. Okay. Now --
MR. THORNBURGH: I'll go ahead and mark as exhibit -- Exhibit Number 2252...
(Document marked for identification as Exhibit T-2252.)
MR. THORNBURGH: ... the five-year data from the ten-year dog study.
Mr. Thomas.
MR. THOMAS: Can I have a copy, please?

Page 392

MR. THORNBURGH: Yes.
BY MR. THORNBURGH:
Q. I'm sorry. Hold on. Yeah.
Okay. Now, this document is the -- is the five-year data from the ten-year dog study that we've been alluding to all along, right?
A. Yes.
Q. And this is the study that you testified showed cracks in the surface layer, outer surface layer, of the polypropylene sutures, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: As indicated in the reports, right.
BY MR. THORNBURGH:
Q. And this study was -- began in 1985. Do you see that?
A. Yes.
Q. Okay. That -- that's like 16 years after the Postlethwait publication. And presumably by this point, the manufacturers, including Ethicon, had made the necessary changes to their Prolene suture to prevent oxidation, right?
MR. THOMAS: Object to the form of

Page 393

the question; scope.
THE WITNESS: I don't think oxidation was an issue that needed to be corrected.
BY MR. THORNBURGH:
Q. Well, surface cracking was, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: What we were discussing before was fragmentation, and I see that as totally different than observations of surface cracking.
BY MR. THORNBURGH:
Q. Okay.
A. Fragmentation is a growth fragment of the suture. Surface cracking is a very subtle observation of what looks like surface cracking.
Q. You agree with me that by 1985, Ethicon would have added antioxidants, like Santonox R and Procol or Lubrol, to their resin during the manufacturing process to prevent oxidation, right?
A. Antioxidant package was added at the very beginning of the development of the Prolene suture and has remained basically unchanged.
Q. And as we discussed earlier, you agree that the antioxidants, including Santonox R

Page 394

and Lubrol and Procol, can leach out of the mesh or suture fibers into the surrounding tissue of the host, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. I think there's evidence of leaching.
BY MR. THORNBURGH:
Q. All right. And in this study, despite the antioxidants being added to the Prolene sutures, the surface layer or outer surface of the polypropylene fibers cracked, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I want to look at the details of the report and...
BY MR. THORNBURGH:
Q. Did you see this before today?
A. Yes.
Q. Okay.
A. I've not memorized every paragraph.
Q. Let's go through it together.
MR. THOMAS: Well, wait. There was a question pending. Do you want to withdraw it and ask another?

BY MR. THORNBURGH:
Q. I think the question was...
MR. THOMAS: Your question at 91, 11.
BY MR. THORNBURGH:
Q. In this study, despite the antioxidants being added to the Prolene sutures, the surface there or outer surface of the polypropylene fibers cracked, correct?
MR. THOMAS: He never answered that question.
THE WITNESS: Yes, and I want to take a look at the report so I can recall just what was written, because I am trying to reflect the report.
BY MR. THORNBURGH:
Q. Well, we can go through it together to help you answer that question.
A. I am looking at the bottom of ETH.MESH.11336475, and looking at the conclusions, and then it says out of seven Prolene explants, two revealed cracking.
Q. So the answer to my question is yes.
MR. THOMAS: Object to the form of the question.
THE WITNESS: This is a complete answer.

BY MR. THORNBURGH:
Q. Despite the antioxidants being added to the Prolene sutures, in two of the Prolene sutures in the study, the surface layer was cracked, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Two revealed cracking, yes.
BY MR. THORNBURGH:
Q. And you aren't suggesting to the ladies and gentlemen of the jury that those cracks were anything other than the Prolene polypropylene, are you?
A. No, I am not suggesting that, and that's not reflected in this report.
Q. You would agree that the surface layer that's cracked here is the polypropylene surface layer, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: In reading the report, it says that -- that's what I would conclude.
BY MR. THORNBURGH:
Q. And if we look back up at the results

and discussion section, on Page 2 of Exhibit Number 2252, which is the five-year data, the investigator and author of this report writes that: A table is included in this report which summarizes the light microscopical observations. It can be said unequivocally that the cracking that was seen in any of the sutures was not introduced by sample preparation, i.e., drying.
If cracking was observed on a dry suture in the light microscope or in the SEM -- scanning electron microscopy -- the same cracking is also found on the same suture after it had been in body fluids and then in sterile water without ever having dried.
So this reporter, the researcher at Ethicon, wrote that it can be said unequivocally that the cracks were not caused by the introduction by sample preparation, right?
A. Yes. That's what it says.
Q. And if we go to -- on the same page, if we go to the third section regarding SEM, scanning electronic microscopy, of PVDF explants, it was found that no cracking or abrasions were found on the PVDF sutures, correct?
A. Yes. At this interval, that's

correct.
Q. But at this five-year interval, the scanning electron microscopy of Prolene explants on explants from dogs 2012 and 2018, a few cracked areas were observed. Both of these sutures came from Site 4. Do you see that?
A. Yes.
Q. And the conclusion that we discussed a moment ago was that after five years in vivo, the PVDF -- do you know what PVDF is?
A. Yes.
Q. That's a more stable, more inert fiber, isn't it?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. It's a polymer?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: It is a very resistant to degradation kind of polymer and resistant to mechanical damage.
BY MR. THORNBURGH:
Q. More so than Prolene, correct?
MR. THOMAS: Object to the form of

the question; scope.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. And the conclusion was that after five years in vivo, the PVDF 5-0 suture was the only explanted material from the five dogs which did not show any surface damage due to degradation. Out of seven Prolene explants, two revealed cracking.
So in this study, at the five year -- the two-year data in this study didn't show evidence of cracking, but the five-year data, the long-term data, showed evidence of cracking of the Prolene sutures, correct?
A. Yes. That's what it says.
Q. And here is the table that was referenced by the study investigator which shows cracking on the Prolene fibers. Do you see that?
A. Yes.
Q. Finally, on ETH.MESH. number ending in 6483, there are -- there is SEM images, though they're black and white, they show the cracking that was observed in the five-year data. Do you see that?
MR. THOMAS: What page are you on? I'm sorry.

MR. THORNBURGH: ETH.MESH.6483.
BY MR. THORNBURGH:
Q. This is an upside down page, for some reason, but --
A. Yes. I see it.
Q. -- if you see Figure 6, Prolene explants, you can see the cracking, even in this poor copy image, of the Prolene polypropylene that was cracked on the surface of the sutures, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. I see that.
BY MR. THORNBURGH:
Q. Figure 4, ETH.MESH.6481, we have the PVDF explants, which you testified was a more inert polymer than polypropylene and Prolene polypropylene, which shows, really, fibers that look almost pristine, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. No crack, no surface cracking on the PVDF?
MR. THOMAS: Same objection.

THE WITNESS: None shown.
BY MR. THORNBURGH:
Q. Which would be consistent with your testimony that the PVDF polymer is a more inert polymer than Prolene polypropylene?
MR. THOMAS: Object to the form of the question; scope.
BY MR. THORNBURGH:
Q. Right?
A. Yes.
Q. Finally, if we go to the conclusion page on the five-year data, ETH.MESH.11336487, the conclusion here is that after five years in vivo, the PVDF 5-0 suture was the only explanted material from five dogs which did not show any surface damage due to degradation.
So here the study author is discussing degradation, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. It's as stated.
BY MR. THORNBURGH:
Q. And included in his analysis of degradation is his observation that the Prolene explants did show signs of degradation as a result

of the surface cracking on the outer layer of the polymer, correct?
A. As reported.
Q. Correct? Yes?
A. Yes.
Q. Now, this study and the findings in the study showing that the polypropylene can crack on the surface of the Prolene sutures was conducted nine -- approximately nine -- eight or nine years prior to the marketing of TVT, correct?
A. Yes. August 10, 1990 is the date of the report.
Q. And prior to Ethicon's claim in the 1999 label that the material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes, correct?
A. One cannot look at this -- this observation.
Q. Yes or no, sir.
A. I can't give a "yes" or "no" answer.
Q. It's a really easy question.
A. No, it's not.
Q. The study -- the 1990 study was conducted nine years before the 1990 label which included the claim that the material is not

Page 403

absorbed, nor is it subject to degradation or weakening by action of tissue enzymes, correct?

MR. THOMAS: He's just asking you now about the date, Tom, nothing more.

THE WITNESS: The date is August 10, 1990.

BY MR. THORNBURGH:

Q. Nine years prior to this claim in the IFU, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Yes.

MR. THORNBURGH: Let's go ahead and mark the seven-year data.

(Document marked for identification as Exhibit T-2253.)

BY MR. THORNBURGH:

Q. I marked the seven-year data ETH.MESH.11336034 as Exhibit 2253.

Doctor, you've had an opportunity prior to coming into this room for your deposition to review the seven-year data for the ten-year Prolene dog study, correct?

A. Yes.

Q. And the seven-year data --

Page 404

MR. THOMAS: Just --

MR. THORNBURGH: Sorry?

MR. THOMAS: There's additional data reported at seven years. This is not the totality of the data. I wanted to make sure that you weren't representing that to be the totality of the data.

MR. THORNBURGH: Well, that's -- in the report. This is the report.

MR. THOMAS: It's not the totality of the data. There's seven-year data that's also been produced to you.

MR. THORNBURGH: Well, I understand that. I understand that. We're going to talk about this report currently, and if there's a need to, I'll go to the other -- the other additional data. I don't know that there's a need to do that, but we'll get there, Dave. Don't worry.

And if I don't cover something that you think is important, Dave, you'll have a chance to make those representations to the jury during your cross-examination or direct examination.

BY MR. THORNBURGH:

Q. Dr. Barbolt, October 15, 1992, that again is several years prior to the claim that was made in the IFU that we looked at that the material

Page 405

is not absorbed, nor is it subject to degradation or weakening by action of tissue enzymes. Correct?

A. Yes.

Q. And additional studies were performed on the Prolene sutures at this seven-year interval, correct?

For example, IR microscopy was used to examine cracked areas in Ethilon, Novofil, and Prolene explants. And the conclusion written here or the findings summarized here is that the IR spectra obtained for cracked Prolene specimens, Figure A, showed possible evidence of slight oxidation with a broadened weak absorbance at about the 1560 range. Do you see that?

MR. THOMAS: 1650 range.

BY MR. THORNBURGH:

Q. Yeah, 1650 range.

A. Yes.

Q. You see that, right?

A. Yes.

Q. So not only were -- did the sutures show evidence of surface cracking, but the IR spectra also showed that there was evidence of oxidation?

MR. THOMAS: Object to the form of

Page 406

the question.

Read the complete sentence, please.

MR. THORNBURGH: Dave, you'll have a chance to make representations. I am showing the jury IR spectra obtained for cracked Prolene specimen showed possible evidence of slight oxidation.

MR. THOMAS: That is a proper reading --

MR. THORNBURGH: Move to strike your -- move to strike your -- Dave, if you're going to try to make these speaking objections and suggesting answers to the witness, then I am going to call the Judge.

MR. THOMAS: You call the Judge --

MR. THORNBURGH: Okay?

MR. THOMAS: -- because you are representing this to be something else.

MR. THORNBURGH: Because speaking objections -- because speaking objections are inappropriate. The question remains especially when they suggest answers -- okay?

MR. THOMAS: I certainly know the rules, Dan. I certainly know the rules. Thank you. Let's move on.

BY MR. THORNBURGH:
Q. IR spectra showed possible evidence of slight oxidation, correct?
A. Yes.
Q. Okay. Now, there's also an observation regarding the other Ethilon and Novofil, which differed from uncracked areas. And the conclusion was, expected IR absorbances for oxidation would be masked by strong carbonyl absorbances normally observed in these sutures.
So there's a discussion here that -- of the -- what would be expected to be seen could be masked by strong carbonyl absorbances. Do you see that?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. And at the seven-year data, Ethicon's investigator found degradation in Prolene is still increasing in PVDF -- even though a few cracks were found, is still by far the most surface resistant in-house made suture in terms of cracking.
That's the findings by Ethicon's investigator, right?

A. Yes.
Q. An employee for Ethicon who actually investigated degradation of Prolene sutures and came to the conclusion that degradation is occurring in Prolene, right?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. Do you see that?
A. Yes, I see that. Surface degradation, and they're making a reference to surface degradation. Yep. I see it.
Q. So you agree as the person for Ethicon who's looked at these studies that surface degradation can occur on the Prolene polypropylene, correct?
A. That was a surface change observed in this report and so reported.
Q. And so you agree that surface degradation can occur in the Prolene polypropylene that's contained in the TVT meshes, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That's the data in this report reflecting the SEM parameters evaluated.

BY MR. THORNBURGH:
Q. And that's Ethicon's position as you -- as the spokesperson for Ethicon, it's Ethicon's position that degradation, surface degradation, can occur, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. And this was known well in advance of this statement that the material is not absorbed, nor is it subject to degradation, correct?
A. Yes. This is from 1992.
MR. THORNBURGH: Okay. Lunch break.
THE VIDEOGRAPHER: We're now going off the video record. It's 11:48.
(Lunch break.)
THE VIDEOGRAPHER: We're back on the video record. It's now 12:43.
BY MR. THORNBURGH:
Q. Now, Doctor, I'd like to turn your attention back to the e-mail that we began to discuss earlier in your deposition, Exhibit Number T 4012.
(Whereupon, a discussion was held off

the record.)
THE WITNESS: Okay.
BY MR. THORNBURGH:
Q. Now, this e-mail --
MR. THOMAS: Give me just a half a second to get back on the same page.
Thank you. I am ready.
BY MR. THORNBURGH:
Q. This e-mail is again from Dr. Divilio, and you were copied on this e-mail, right?
A. Yes.
Q. In 2007, correct?
A. Yes.
Q. And the e-mail says: Bruce Ramshaw from the University of Missouri is challenging our perception of polypropylene as an inert material after implantation. In a recent article, his group looked at explanted polypropylene from a Bard Composix mesh under EM, electron microscopy, and found that the surface of the fibers had been altered with respect to the pristine material with evidence of blistering and increased surface roughness, possibly due to oxidation.
Now, this is the same finding or

Page 411

similar findings, at the very least, that were made in the five-year and seven-year, ten-year dog study, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: No. In that study, there was descriptions like surface cracking. I don't see that here.

BY MR. THORNBURGH:

Q. Well, it says: The surface of the fibers had been altered with respect to the pristine material.

That could include and would include surface cracking, wouldn't it?

MR. THOMAS: Object to the form of the question.

THE WITNESS: As I read forward, it says -- and they define what they mean by alteration by saying evidence of blistering and increased surface roughness, possibly due to oxidation.

BY MR. THORNBURGH:

Q. Like surface cracking, sir, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: I see that the words

Page 412

are different.

BY MR. THORNBURGH:

Q. Nevertheless, it goes on to write: We previously had implanted Prolene suture into dogs, and explants after ten years revealed no changes in the material.

That's not a true statement, is it?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Well, as we discussed, there were some changes that were observed on the surface.

BY MR. THORNBURGH:

Q. Surface degradation, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: I think that's part of that report.

BY MR. THORNBURGH:

Q. So that's not a true statement, that Ethicon had not seen changes in the material, in the ten-year data, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Well, where there were

Page 413

no changes were in molecular weight and tensile strength. So they might have been in this memo making reference to the more important quantitative parameters like molecular weight and tensile strength.

BY MR. THORNBURGH:

Q. Well, Dan Burkley found in the seven-year data that there was degradation in the Prolene, right?

MR. THOMAS: Object to the form of the question.

THE WITNESS: That's in the report. That's an observation. That's a component of the parameters investigated in this study.

BY MR. THORNBURGH:

Q. The statement made by Dr. Divilio that we had previously implanted Prolene suture into dogs, and explants after ten years revealed no changes in the material, is not a completely true statement, is it?

MR. THOMAS: Object to the form of the question.

THE WITNESS: I don't know what he meant by that statement. I can't speak for him.

BY MR. THORNBURGH:

Page 414

Q. Well, there are certainly changes seen by Dan Burkley in the study, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Surface changes were observed.

BY MR. THORNBURGH:

Q. Degradation was observed, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: As noted in the report.

BY MR. THORNBURGH:

Q. Degradation was observed? Yes or no?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Could you pull up that previous screen?

BY MR. THORNBURGH:

Q. Degradation in Prolene?

A. Yes.

Q. The e-mail goes on by Dr. Divilio, who says: I am wondering if the effects that Ramshaw, et al., are seeing are due to the abrasions of fiber against fiber in a mesh construct due to flexing that occurs after implantation, trauma to

Page 415

the mesh as a result of implantation from a patient, or actual oxidation. I think it's important that we understand what they're seeing, as this group has a well-funded lab that will be looking at explanted mesh in great volume over the next couple of years, and our current concepts are going to be challenged.

Do you see that there?

A. Yes.

Q. Do you recall this e-mail?

A. No, I do not, although it's important to note that they're talking about Bard Composix mesh, which is a multi-component mesh, and it's not Prolene polypropylene mesh.

Q. Well, you're familiar with the Costello studies that found degradation of the polypropylene, correct?

MR. THOMAS: Object to the form of the question.

BY MR. THORNBURGH:

Q. You understand that Costello was working with the Ramshaw group?

MR. THOMAS: Object to the form of the question.

THE WITNESS: I am trying to recall the detail. Let's look at the Costello paper.

Page 416

BY MR. THORNBURGH:

Q. Well, I'm just asking you -- we'll look at the Costello paper.

A. Okay. Okay.

Q. I'm asking you: Are you aware sitting here right now, based on your memory, whether or not the polypropylene in the Costello study showed evidence of surface degradation?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: First, I thought it was the Bard product. You can correct me --

BY MR. THORNBURGH:

Q. Polypropylene. My question to you is polypropylene.

A. Polypropylene -- polypropylenes are not generic substances. They're very different, depending on an additive package that's required to provide stabilization, manufacturing process, aid, so on and so forth. So I would not equate Prolene polypropylene with any other manufacturer's polypropylene.

Q. Like the additive package in the Prolene?

MR. THOMAS: What's the question? I

Page 417

don't understand the question. Object to the form of the question.

BY MR. THORNBURGH:

Q. You're talking about generic with respect to additive packages. You'd agree that the Prolene that was used in the seven -- the five-year, ten-year results, and the seven-year, ten-year dog results also had the antioxidant additives, correct?

A. Yes, and I believe the additive package is what prevented a loss of molecular weight and tensile strength.

Q. It didn't prevent surface degradation, did it?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Well, there is evidence that it did not.

BY MR. THORNBURGH:

Q. So Dr. Dieter -- am I pronouncing his name correctly?

A. Dieter Engel.

Q. Dieter Engel? Dr. Engel, he's a doctor from Germany, right?

A. He was head of the R&D group for a while.

Page 418

Q. For Ethicon, correct?

A. Yes.

Q. And Dr. Engel, on July 6, 2007, responds. And you're copied on this e-mail, right? Do you see that?

A. Yes.

Q. Tom, thanks for checking back and asking for my scientific perspective.

There have been a number of anecdotal reports that polypropylene mesh shows some changes in the surface with time, including Ethicon's own internal studies.

Correct?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Anecdotal reports?

BY MR. THORNBURGH:

Q. You'd agree that the seven-year -- the five-year data and seven-year data from the ten-year dog studies isn't anecdotal; that's an actual scientific experiment that found surface degradation. Correct?

A. Yes. There were observations of surface cracking and degradation.

Q. Dr. Engel goes on to say the Aachen

Page 419

group -- which would include Doctors -- Professors Klinge and Klosterhalfen, right?
A. Yes. They were with the Aachen group for some time.
Q. The Aachen group, who has so far collected more than a thousand explanted meshes, showed examples many years back. Do you see that?
A. Yes.
Q. You understand, don't you, that the Aachen group, including Klinge and Klosterhalfen, were consultants paid by Ethicon to evaluate polypropylene meshes, don't you?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That's my understanding.
BY MR. THORNBURGH:
Q. And when -- during the time that Dr. Klosterhalfen was a consultant for Ethicon, he evaluated a thousand explanted meshes which also showed degradation?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. Do you understand that, sir?

Page 420

A. These are human -- I am understanding that they're human explants that he's then investigated. I don't know who the manufacturers were, what products they were, but I see the statement, and it stands as is.
Q. Human explants evaluating who?
Human explants will provide more reliable clinical evidence, both of degradation and the materials than your animal studies, won't they?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: No. No, I do not believe that, because, typically, these are meshes or products explanted for a particular reason. Likely, they failed. It could be an infected site.
The best way in a preclinical way to understand the intrinsic characteristics of materials is to implant them in very controlled animal model systems.
BY MR. THORNBURGH:
Q. Did you ever look at any explanted meshes from humans?
A. No, other than photographs or photo micrographs and publications discussing such cases.
Q. Dr. Engel says: We did different

Page 421

tests in-house with accelerated aging, too, and found microscopic changes in the surface of the mesh fibers.
So there are additional studies according to Dr. Engel of -- by Ethicon which also showed surface degradation, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. He's talking about accelerated aging in conditions of increased temperature with the intention to increase any impacts of aging.
BY MR. THORNBURGH:
Q. Did you include any of those in-house accelerated aging studies in your list of studies regarding degradation that found microscopic changes in the surface of the mesh?
A. I am not aware of them. I did not include it in any of these documents.
Q. In fact, you did not include those studies in your material related to this question of degradation, did you?
MR. THOMAS: Object to the form of the question; asked and answered.
THE WITNESS: I just said that. I

Page 422

just said that.
BY MR. THORNBURGH:
Q. Why didn't you include those studies in your list --
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. -- or in your binder regarding the statement or the claims by Ethicon that the Prolene in the TVT will not degrade?
A. The literature searches conducted that form the basis for the documents that are compiled here were a search of the Ethicon corporate R&D central files. I was not aware of any studies done in Germany that might have impact or contribute knowledge about these topics. If I had, they would have been included.
Q. They're not included, correct?
MR. THOMAS: Object to the form of the question; asked and answered.
BY MR. THORNBURGH:
Q. You haven't even had a chance to review those studies, have you?
A. Well, the first question is that I have not -- they're not included.

Page 423

And the second, I've not reviewed them.
MR. THORNBURGH: Counsel, I'd like production of these in-house studies that showed microscopic changes in the surface of the mesh fibers using the accelerated aging method.
MR. THOMAS: As I told you yesterday at the conclusion of the deposition, if you'd remind me what you've asked me for, we'll respond appropriately.
MR. THORNBURGH: I had to make a note so I could remember to remind you to produce those.
MR. THOMAS: I won't do it unless you remind me. I'll forget.
MR. THORNBURGH: Well, they should have been produced already.
MR. THOMAS: Please.
MR. THORNBURGH: Well, they should have.
BY MR. THORNBURGH:
Q. We did different tests in-house with accelerated aging, too, and found microscopic changes in the surface of the mesh fiber.
What is happening is related to the specific stretching of the fibers when producing

Page 424

sutures. As you know, you have to stretch the fibers to a very high degree to get the required breaking strength. That leads to a very high orientation of the polymer chains and, in turn, makes the surface, the outer fibrils of material relatively susceptible to damage from mechanical stress.
Do you see that?
A. Yes.
Q. You haven't looked at those studies, have you?
A. No.
Q. He goes on to write: All in all, I believe we understand the mechanism pretty well and wouldn't suggest to generate extra data.
Do you see that?
A. Yes.
Q. Were you told by Ethicon -- you were included as part of this e-mail string. Were you told not to generate additional data regarding the potential degradation of Prolene polypropylene meshes?
MR. THOMAS: Object to the form of the question.
THE WITNESS: No.

Page 425

BY MR. THORNBURGH:
Q. Well, this would certainly indicate that Dr. Engel is requesting that no additional studies be done to generate extra data, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. And with good reason.
BY MR. THORNBURGH:
Q. Because you already knew that the surface layer of Prolene polypropylene is susceptible to surface degradation, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: No. He says we understand the mechanism pretty well. No need to do further studies.
BY MR. THORNBURGH:
Q. Because Ethicon already knew that the surface layer of Prolene polypropylene is susceptible to surface degradation, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes.
BY MR. THORNBURGH:

Page 426

Q. What is the future? We will change the material of our mesh and move to Pronova as the future material platform for mesh. Pronova has a reduced foreign body reaction compared to Prolene, as shown in several animal studies.
Did you include the animal studies that showed that Pronova has a reduced foreign body reaction compared to Prolene in any of the studies you list in any of the binders that you brought with you today?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Yes. I've included three studies, one looking at Pronova suture compared to Prolene suture and Dormier repair in rabbits, intramuscular implantation study for six months in rats, and ophthalmic tissue reaction studies for 90 days in rats.
BY MR. THORNBURGH:
Q. Do you agree that with this statement, that Pronova has reduced foreign body reaction compared to Prolene --
A. No, I did not.
Q. -- as shown in several animal studies conducted by Ethicon?

Page 427

MR. THOMAS: Object to the form of the question.
THE WITNESS: I've not seen those studies. The three studies that Ethicon has conducted that I just mentioned show comparable tissue reaction to Prolene suture.
BY MR. THORNBURGH:
Q. You did not include in any of your binders that you brought with you the several animal studies that show that Pronova has reduced foreign body reaction compared to Prolene, did you, sir?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: I don't know the details of these studies. Standard biocompatibility studies were done looking at tissue reaction to Pronova suture compared to Prolene.
These studies may be surgical functionality studies with different prototype meshes. I don't know. I can't respond to that question specifically unless I see the studies that he's making.
BY MR. THORNBURGH:
Q. This really is a "yes" or "no" question.

Page 428

A. No, it's not.
Q. You did not provide in any of the binders that you brought with you today the studies, the several animal studies, that show that Pronova has a reduced foreign body reaction compared to Prolene, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. He goes on to say that Pronova will improve the perceived biocompatibility of our mesh.
Do you see that?
A. Yes, I see that, but don't agree.
Q. Of course.
A. We've got three studies that demonstrate that the tissue reaction to Prolene suture is comparable to Prolene -- to Pronova suture.
Q. You haven't even seen the studies that Dr. Engel is referring to that show that Pronova has a reduced foreign body reaction.
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: That's correct.

Page 429

BY MR. THORNBURGH:
Q. You haven't considered those studies before you walked in today as the person most knowledgeable about the tissue response and tissue reaction, correct?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Studies to support the biocompatibility of Pronova suture were conducted in comparison to Prolene suture in a standard tissue reaction study, a protocol, as required by ISO 10993, Part 1, and G95 FDA guidance on biocompatibility testing.
BY MR. THORNBURGH:
Q. And --
A. And other studies that might have been conducted for other purposes, I don't know. They're not necessary to support the biocompatibility of -- of a Pronova suture. But there are other studies that that have been conducted.
If they provide evidence to counter the study results from the three Pronova studies that I've just mentioned, I'll be glad to look at those.

Page 430

Q. So the answer to my question is that you have not considered before you walked in here today the Pronova studies that showed less foreign body reaction and better biocompatibility, correct?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: I'd have to look at those studies to make that conclusion.
BY MR. THORNBURGH:
Q. You didn't look at those studies before you walked in here today, did you?
MR. THOMAS: Object to the form of the question.
THE WITNESS: No, I did not.
BY MR. THORNBURGH:
Q. Besides, Pronova is much less susceptible to mechanical damage.
As you testified to earlier, PVDF, which is part of the copolymer of Pronova, is a more inert, more stable material than Prolene, correct?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. It is much easier to process in the

Page 431

knitting machine, less quality issues. Do you see that?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. Did you talk to -- as the person that was designated as the person most knowledgeable under the designated topics, did you talk to Dr. Engel about his experience with PVDF sutures and Prolene sutures and that Prolene sutures induce a greater inflammatory response than Pronova or PVDF?
MR. THOMAS: Object to the form of the question.
THE WITNESS: No.
BY MR. THORNBURGH:
Q. Don't you -- you agree as a scientist that generation of data that could help better answer questions, safety questions, is important, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That's why we have 18 binders of studies surrounding us that contain studies conducted in the mid 1960s.

Page 432

BY MR. THORNBURGH:
Q. Vast --
A. And continue to this day.
Q. Vast majority of those are suture studies, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: We'd have to do the exercise.
BY MR. THORNBURGH:
Q. You didn't do the exercise before you came in here today?
A. No. I didn't think it necessary, because I believe that the data that's generated for suture containing the same Prolene polypropylene fiber as in mesh are directly applicable and relevant.
Q. General scientific principle: The greater the surface area of an implanted medical device, the greater the inflammatory response.
MR. THOMAS: Object to the form of the question.
THE WITNESS: There's some relationship to increased surface area and increasing tissue action, because that's the

Page 433

interface between implanted material and surrounding tissue.
THE VIDEOGRAPHER: I've got to change the tape.
It's now 1:08. Going off the video record.
This concludes Volume 2, Tape 2 of the videotape deposition of Dr. Thomas A. Barbolt.
(Short break.)
THE VIDEOGRAPHER: We're back on the video record. It's 1:14.
This begins Volume 2, Tape Number 3 in the videotape deposition of Dr. Thomas A. Barbolt.
BY MR. THORNBURGH:
Q. Dr. Barbolt, we talked briefly about Dr. Ramshaw and Dr. Costello. Do you remember that?
A. Yes.
Q. And your e-mail -- the e-mail that you were included on discussed studies that were done by Ramshaw's group that found degradation of polypropylene?
A. Yes.
Q. And you had indicated that you had reviewed this study, correct?

Page 434

MR. THOMAS: Object to the form of the question. It's not in preparation for this deposition.
BY MR. THORNBURGH:
Q. Are you not prepared to talk about the Costello studies?
A. No. That's not one of the studies that I brought with me today.
Q. Just so the record is clear, because I think you were indicating that maybe it was the -- because there was a composite mesh that may have been studied, that you weren't aware whether or not that was polypropylene, so I just want to point out in the record this conclusion.
Overall, the results support our hypothesis that in vivo -- inside the body, right?
A. Yes.
Q. -- oxidation plays a role in the degradation of polypropylene.
Do you see that?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. And as I pointed out earlier, that's not Prolene polypropylene. That's Bard polypropylene.

Page 435

BY MR. THORNBURGH:
Q. Well, it's polypropylene, nonetheless.
A. There's a big difference, because as we discussed earlier, polypropylene without an appropriate antioxidant package is susceptible to degradation. And if you add an appropriate antioxidant package, it is resistant to oxidation.
Q. Well, we know from the ten-year -- the five-year data, from the ten-year dog study, Ethicon study, seven-year data from that study, the Prolene polypropylene was susceptible to surface cracking, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: It was susceptible to surface cracking, but it did not result in loss of molecular weight or impact on tensile strength, key mechanical properties of polypropylene fibers.
BY MR. THORNBURGH:
Q. In this statement, in this claim in the IFU, it doesn't say that the material is susceptible to surface degradation, does it?
MR. THOMAS: Object to the form of the question.

Page 436

THE WITNESS: No, it does not.
This is an instructions for use. It's trying to relay to the end user of the product important information, and for surgeons. No matter surface changes -- if there's no impact on molecular weight or tensile strength, the surface changes are of no consequence.
BY MR. THORNBURGH:
Q. This is important -- the IFU provides important information to physicians, correct?
MR. THOMAS: Object to the form of the question; scope.
BY MR. THORNBURGH:
Q. That's what they just said, right?
A. It's intended to relay to the end users, the surgeons, information that they would find most useful.
Q. And Ethicon did not relay any information to the physicians in this IFU that the Prolene in the TVT mesh is susceptible to surface degradation, did they?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That is not useful information in light of no impact on molecular

Page 437

weight or tensile -- tensile testing. That's the kind of information that's useful to surgeons, not any other observations that might be observed but don't translate into significant impact on mechanical characteristics.
BY MR. THORNBURGH:
Q. That's absurd.
MR. THOMAS: Excuse me.
BY MR. THORNBURGH:
Q. You're not even -- you're not a clinician, are you?
MR. THOMAS: Please. Stop, stop. Stop.
Thomas, let's take a break.
BY MR. THORNBURGH:
Q. You're not a clinician, are you?
MR. THOMAS: Back up. Don't tell my witness his testimony is absurd. You can ask questions and get your answers, and we'll object to form, but you just ask him straight questions, and you'll get straight answers.
BY MR. THORNBURGH:
Q. You're not a medical doctor, are you?
A. That's correct.
Q. You've never treated patients, have

Page 438

you?
A. Of course not.
Q. You've never looked at an IFU and relied on an IFU in having a risk/benefit discussion with patients, have you?
A. That's not my role in preclinical.
Q. But, yet, you're here telling the ladies and gentlemen of the jury that information about the surface degradation of Prolene that's implanted permanently in women -- women's pelvises, is not important?
MR. THOMAS: Excuse me.
BY MR. THORNBURGH:
Q. That's the position that you took?
MR. THOMAS: You're arguing with the witness.
MR. THORNBURGH: I am not.
MR. THOMAS: Yes, you are. And we're not going to argue with him. And I object to the form of the question.
BY MR. THORNBURGH:
Q. You're taking the position on behalf of Ethicon --
MR. THOMAS: His position has been taken. His answer has been given.

BY MR. THORNBURGH:
Q. You're taking the position --
MR. THORNBURGH: Dave, you can object.
MR. THOMAS: You're asking the same question three times.
MR. THORNBURGH: Dave, you can object.
MR. THOMAS: I can stop the deposition, too.
MR. THORNBURGH: Dave, you can object.
BY MR. THORNBURGH:
Q. Mr. Barbolt, you're taking this position as the company spokesperson for Ethicon that information about surface degradation is not important to clinicians when they're relying on the information for use and having risk/benefit discussions with their patients who will be implanted with this medical device for the rest of their lives in their -- in and around their sexual and reproductive organs. That's the position?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: The IFU is not the

responsibility of folks in preclinical. The IFU is put together by regulatory and medical professionals gathering input from all areas of manufacturing, preclinical, physical testing, whatever is necessary in their minds to provide the most useful information to the end users as possible.
BY MR. THORNBURGH:
Q. So would you defer to a clinician about whether or not information about surface degradation of products that are being implanted permanently in and around the sexual and reproductive organs of women is important information to have?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Would I defer to clinicians to make that judgment? With the information that's been provided in this case by preclinical relating to three things in that study; one, observations of surface degradation; two, quantitative measurements of molecular weight; and, three, quantitative measures of tensile strength.
Molecular weight and tensile strength testing indicate there's no evidence of degradation.
MR. THORNBURGH: Move to strike;

nonresponsive.
MR. THOMAS: Did you finish your answer? Did you finish your answer?
THE WITNESS: Yes.
MR. THOMAS: Okay. Thank you.
BY MR. THORNBURGH:
Q. You defer to a clinician about whether or not surface degradation is important information that they need when having a risk/benefit discussion with their patients, correct?
A. I think a preclinical scientist will always defer to a clinician in making those judgments with patients.
Q. You made a statement earlier, general scientific principle, that medical devices with a larger, greater surface area will have a greater inflammatory response than one with a lower surface area. Do you remember that statement?
A. Yes. And let me --
Q. General scientific principle, right?
A. Right. And let me remind you. It's a general scientific principle. And the exact tissue reaction to an implant needs to be determined by an implantation study, the results of which will

overrule any general scientific principle and will rely on the specifics of real and actual data generated from a study.
Q. And in this study regarding surface area, these investigators, who actually, by the way, study degradation, found that degradation -- that in vivo oxidation plays a role in the degradation of polypropylene hernia mesh materials and that there may be a difference in the degree of oxidation between a heavyweight material and a lightweight material because of a reduced inflammatory response.
Do you see that?
MR. THOMAS: Object to the form of the question.
THE WITNESS: This is not an Ethicon product.
BY MR. THORNBURGH:
Q. That wasn't the question.
A. I am here to talk about Ethicon products.
Q. Polypropylene is contained within Ethicon products, correct?
A. As I indicated earlier, all polypropylenes are not the same. Polypropylenes with no additive package are susceptible to

Page 443

oxidation. And I got to imagine that polypropylene resin with varying kinds of antioxidant packages would have varying protective actions against oxidation.

Q. These are antioxidants that you testified earlier that there's evidence that those additives leach out of the polypropylene that's used in the TVT devices, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Yes. I think there's evidence that they leak out.

BY MR. THORNBURGH:

Q. And would you agree that there would be a difference in the degree of oxidation between a heavyweight material and a lightweight material because of the reduced inflammatory response as a result of a reduction in the surface area that we discussed earlier?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: It's a theoretical -- it is a theoretical discussion.

BY MR. THORNBURGH:

Q. Yes or no?

Page 444

A. I don't know what materials they're talking about. I don't know what additive packages they're talking about.

Q. How about polypropylene?

MR. THOMAS: Excuse me. Let's slow down a little bit. You're running into each other, and the record is terrible, and I don't get a chance to object, and I need my chance to object. Let's slow down so everybody gets a chance to say what they need to say.

MR. THORNBURGH: I'll withdraw and move to strike everything after, it's a theoretical discussion.

MR. THOMAS: Excuse me. I need to say something.

I said the record is terrible. I should have said we risk creating a terrible record, because I am confident that our court reporter is doing absolutely the best that she can.

MR. THORNBURGH: Off the record for a moment.

THE VIDEOGRAPHER: Off the video record, 1:26.

(Short break.)

THE VIDEOGRAPHER: Back on the video

Page 445

record. It's 1:34.

BY MR. THORNBURGH:

Q. Dr. Barbolt, you've also been designated by Ethicon to discuss or testify regarding the specifics of all testing related to the TVT products during the design and development stages, including but not limited to leaching, correct?

A. Yes.

MR. THOMAS: Do you want those notebooks now?

MR. THORNBURGH: I don't know that we necessarily need all of them, so why don't we -- why don't we move forward, and if we need them, we'll --

THE WITNESS: Let me get this first one, which is an index. They're -- the index is all the same.

BY MR. THORNBURGH:

Q. So let's -- first let's talk about the submission to the FDA, October of 1997, the five -- the 510(k) for the TVT-Retropubic.

Did you bring that with you today?

MR. THOMAS: Maybe. Do you have one handy?

MR. THORNBURGH: I think I do.

Page 446

THE WITNESS: Do you want to bring up the --

MR. THOMAS: Let him give you one.

THE WITNESS: Okay. Okay.

BY MR. THORNBURGH:

Q. It's been premarked as Exhibit Number T-2017. The Bates number is ETH.MESH.00019863.

Now, before I get into the discussion about the topics and studies regarding leaching --

MR. THOMAS: I'm sorry. This begins with Attachment 5. And the bottom of it says Page 3 of 69. Do you know if this was the complete --

MR. THORNBURGH: Oh, you know what? Sorry. I may have given you the wrong --

If you want to give that back to me. I am not exactly sure what I just handed you there.

MR. THOMAS: Me either.

BY MR. THORNBURGH:

Q. Okay. Let's do this again. I am going to hand you what's been premarked as Exhibit Number 2105, which is related to the 510(k) submission regarding the TVT-Retropubic system.

MR. THOMAS: May I have one, please?

MR. THORNBURGH: Yes.

MR. THOMAS: Thank you. This one is highlighted. Is it supposed to be?
MR. THORNBURGH: That's okay.
BY MR. THORNBURGH:
Q. Now, this is a submission that Ethicon made to the FDA regarding the TVT device, correct?
A. Yes. That's what it looks like.
Q. And before we get into a discussion about the cytotoxicity testing and the leaching issues, I just want to turn your attention to ETH.MESH.00371515.
A. 515.
Okay.
Q. Now, this is the statement that we've discussed over the last two days regarding minimal inflammatory transitory tissue reaction and that the material is not absorbed, nor is it subject to degradation. Right?
A. Yes.
Q. Now, the statement, the material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes, was provided to the FDA in the 510(k) submission on October 29, 2007, correct?

MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: 2007?
BY MR. THORNBURGH:
Q. I'm sorry. October 29, 1997. Correct?
A. Okay. That would be the time of the submission of the 510(k) for TVT original or retropubic.
Q. Right. So October 29, 1997 Ethicon submitted to the FDA the 510(k) submission related to the TVT-Retropubic, correct?
A. Yes.
Q. And in that submission, Ethicon stated that the material is not absorbed, nor is it subject to degradation.
Do you see that?
A. Yes.
Q. But as we've already established, by 1990 and 1992, Ethicon was aware from its own internal studies that the Prolene in the TVT was subject to surface degradation, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: We've talked a lot

about this before.
BY MR. THORNBURGH:
Q. Correct?
A. And as I indicated before, there were three endpoints in that experiment that are important: Subjective observations, observations by a human being about what's on the surface of the suture, and then quantitative assessments of molecular weight, and quantitative assessments of tensile strength.
In terms of surface changes, surface changes were reported. In terms of molecular weight and tensile strength, no impact on either of those parameters, which would lead one to conclude that there's no evidence of degradation that's meaningful.
MR. THORNBURGH: Move to strike; nonresponsive.
BY MR. THORNBURGH:
Q. Sir, do you think it's okay for Ethicon to misrepresent information in a 510(k) submission to the FDA regarding surface cracking?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I don't think they've

done that.
BY MR. THORNBURGH:
Q. Regarding surface degradation?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I do not think they've done that.
BY MR. THORNBURGH:
Q. This statement says the material is not subject to degradation.
That's what it says, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I've already explained that the IFU is not the responsibility of preclinical science. Preclinical scientists provide information to regulatory folks and medical affairs people and clinicians, their findings. And those folks put together the most useful information for the end user, the surgeon.
BY MR. THORNBURGH:
Q. It would be inappropriate for the FDA to permit -- to misrepresent information about degradation to the FDA, wouldn't it?
MR. THOMAS: Object to the form of

Page 451

the question.
THE WITNESS: I don't think they've done that.
BY MR. THORNBURGH:
Q. Well, the 1990 and 1992 internal studies showed surface degradation of the Prolene mesh, did it not?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I've already explained --
BY MR. THORNBURGH:
Q. Yes or no?
A. I've already explained the -- my reasonings of this in answering this question on a number of occasions. And I can only conclude that the regulatory folks and clinical folks took the sum total of the results from that study and said, you know what? There's no impact on molecular weight. There's no impact on tensile strength. So there's no degradation. And that is what is reflected in this IFU.
Q. That statement, sir, that you just made is inconsistent with the conclusions by the Ethicon employee who wrote that degradation in

Page 452

Prolene is still increasing, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: All degradations are not created equal. Degradations that are important are changes in molecular weight and tensile strength. Anything less than that is uneventful trivial response, a trivial change, that has no impact on important mechanical characteristics like the tensile strength.
BY MR. THORNBURGH:
Q. Do you think -- do you think that surface degradation of Prolene mesh would be unimportant to the FDA?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes, as long as there were no impact on tensile strength and no impact on tissue reaction.
BY MR. THORNBURGH:
Q. You have to agree with me, sir, that if the material is peeling away and coming off of the Prolene fibers, that those -- those shards that peel away will increase or by itself cause an inflammatory response to tissue that it comes in

Page 453

contact with, correct?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. There's a question pending.
MR. THOMAS: He's answered this same question twice today.
THE WITNESS: First -- first, I've not seen the peeling that you're talking about.
And, second, all the data that we've brought here today, some 49 reports, suggest that the tissue reaction to Prolene polypropylene suture in mesh is relatively mild and in some cases reduces in severity over time.
So if there are any peeling off of pieces of the suture, as you would suggest, it's not having an impact on the tissue action.
BY MR. THORNBURGH:
Q. We saw in the Postlethwait paper that even minute fragments can cause independent inflammatory responses, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: The macro fragments that's discussed in the Postlethwait paper are not

Page 454

the same as what you're describing comes off the surface of a Prolene fiber, which we've not seen any of that in the images that we've discussed today.
BY MR. THORNBURGH:
Q. So Ethicon chose not to warn doctors or disclose to the FDA that the Prolene mesh is subject to surface degradation, correct?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Ethicon is trying to provide to the surgeons the totality of the result and the most significant result that they would be concerned about, and that is a breakdown of the polymer chains, which would be reflected in a loss of molecular weight and a loss of tensile strength, which would not be useful for a suture, a single strand suture, that's used for cardiovascular repair, of which surgeons rely on to maintain its tensile strength for the life of the patient.
BY MR. THORNBURGH:
Q. Are you done, sir? Are you done, sir?
Dr. Barbolt, are you finished?
A. Yes.
MR. THORNBURGH: Move to strike;

nonresponsive.
BY MR. THORNBURGH:
Q. Ethicon chose not to warn doctors or to disclose to the FDA that the Prolene mesh is subject to surface degradation in their 510(k) submission, correct?
MR. THOMAS: Object to the form of the question; scope.
He's not designated on this, Dan.
THE WITNESS: It's not in this action section.
BY MR. THORNBURGH:
Q. If I can turn your attention to Bates Number ETH.MESH.00371544, this is the biocompatibility test results, correct?
A. Yes.
Q. And you drafted this, didn't you?
A. This is likely cut and paste from a document that I would have provided, and it's part of a 510(k) submission. This looks like my language.
Q. And on Page 41, ETH.MESH.00371545, there's a discussion about cytotoxicity testing that was performed by Ethicon through NAMSA under the ISO 10993-5 guidelines which showed that

polypropylene mesh was moderate to severely cytotoxic in vitro, correct?
A. Yes.
Q. And the polypropylene mesh component of the sterile sheet -- this is apparently what you wrote -- the polypropylene mesh component of the sterile TVT device was cytotoxic, and only the Elution test suggesting cytotoxic potential in this sensitive test system.
So you would agree with me that based on the Elution test, there was evidence of cytotoxicity in vitro, correct?
A. Yes.
Q. And then you wrote: However, the long history of safe clinical use of polypropylene as mesh and suture products suggest strongly that this material is inherently biocompatible, and the potential cytotoxicity observed is self-limiting.
What do you mean by "self-limiting"?
MR. THOMAS: Object to the form of the question; scope.
Have you established that he wrote this part?
MR. THORNBURGH: He said -- I thought he said it was cut and pasted from something he

wrote.
MR. THOMAS: I don't think he -- I don't believe he cut and pasted.
MR. THORNBURGH: Well, now you're doing another speaking objection.
MR. THOMAS: You asked him about this at length in his last deposition. That's why I remember it so well.
MR. THORNBURGH: Well, the subject matter that he's been designated to discuss is leaching, which is covered by -- which is part of the cytotoxicity, is it not?
MR. THOMAS: But you've asked him what he's done personally so far, and you've covered this at length at the last deposition.
Go ahead. It's your deposition.
BY MR. THORNBURGH:
Q. Sir, are you prepared -- did you prepare for this 30(b)(6) deposition to discuss the cytotoxicity testing that was done at Ethicon?
Are you the person most knowledgeable and have you been prepared on that subject for this 30(b)(6) deposition?
MR. THOMAS: He's been designated on the topic as identified in the notice, and leaching

is one of the topics, and cytotoxicity comes within that topic.
MR. THORNBURGH: Okay.
BY MR. THORNBURGH:
Q. Now, sir, I know that you're here. You've been designated by Ethicon as a company spokesperson to discuss this issue.
Were you the person who wrote this section of the biocompatibility testing results?
A. I'm not certain, but it's likely.
Q. And you wrote that: The long history of safe clinical use of polypropylene as mesh in suture products suggest strongly that the material is inherently biocompatible and that the potential cytotoxicity observed is self-limiting.
What did you mean by "self-limiting"?
A. Not progressive beyond the implantation period. Something that's not likely to exacerbate a tissue reaction response.
Q. You'd agree with me that cytotoxicity, even at the implant level, could increase the inflammatory response, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. If there's death

Page 459

of cells, and it's simply cytotoxicity, if there's death of cells in the tissue surrounding the implant, it's very likely to increase the tissue reaction.
BY MR. THORNBURGH:
Q. And some of the symptoms that you would expect to see if a mesh material or the additives in the mesh material were cytotoxic would be delayed wound healing and ulcerations, correct?
A. Well, certainly delayed wound healing and increased tissue reaction.
The relationship to ulceration is not a direct one. It doesn't usually happen. However, it can occur in some animal studies because of the nature of animals. But the two key endpoints would be increased tissue reaction and delayed wound healing response.
Q. And in the actions animal section of the IFU --
MR. THOMAS: What page are we, please?
MR. THORNBURGH: ETH.MESH.1515 of the exhibit, 2105.
BY MR. THORNBURGH:
Q. In the action section in the animal

Page 460

section of the IFU, there is no disclosure to physicians that there is evidence in vitro tests of cytotoxicity associated with the Prolene mesh in TVT, correct?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: I don't see it here, but as I indicated before, for end users -- and, again, this is not a preclinical document. Preclinical folks provide information for the people responsible for this document.
But in the absence of increased tissue reaction and in the absence of impact on wound healing, there's no need to put additional information in the action section. So that would be my recommendation. And, again, it's the clinicians and regulatory folks who make the final call.
BY MR. THORNBURGH:
Q. Did you make that recommendation -- did Ethicon make that recommendation or did you make that recommendation to the individuals who were deciding on what language goes into the IFU?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I provided the

Page 461

information as you see here, and they made the judgment. I am not sure how -- how that went, where it went, and where they went to get information, but they had access to this information.
BY MR. THORNBURGH:
Q. And that's despite the fact that your study showed the potential, at least in vitro, for cytotoxicity, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. Yes. And at the same time, as I've indicated here, they've relied on clinical data in ETH.MESH.00371546 to address any potential in vivo cytotoxicity by talking about their experience in the field.
BY MR. THORNBURGH:
Q. In fact, I'm going to go ahead and -- I am going to give you what's been premarked as T-3185.
Who's Cary Linsky?
A. I think he was the project leader for TVT original.
MR. THOMAS: Just for the record, this is marked 3186?
MR. THORNBURGH: I'm sorry. Yes.

Page 462

Premarked Exhibit 3186.
BY MR. THORNBURGH:
Q. And this is dated 9/11/97, correct?
A. Yes.
Q. And this discusses how there was a decision to delay the TVT device from August to September as a result of the cytotoxicity results from NAMSA, correct?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: I would have to read this document. I've not seen this before.
Yeah. I see that. I totally agree.
BY MR. THORNBURGH:
Q. It says: The TVT data is vitally important for two reasons. It is the only functionality data we have, i.e., no animal studies. Two, the toxicity position paper draft heavily relies on the clinical data to place in perspective the cytotoxicity profile of the device.
For the above reasons, we need to have good assurance for the integrity of the data that we put into our submission.
Do you see that?
A. Yeah, absolutely. I totally agree.

Page 463

Q. Okay. So there was already a toxicity position paper that was drafted before the clinical data was even available?
MR. THOMAS: Object to the form of the question; scope.
BY MR. THORNBURGH:
Q. Right?
A. Well, the toxicity position paper is independent of any clinical data. It was based on a compilation of all the cytotoxicity studies that were conducted previous to the 510(k) submission and for the 510(k) submission.
So that happens -- that's a preclinical issue that happens independent of clinical.
Q. And the clinical data that Ethicon was waiting on before submitting the 510(k) submission with your biocompatibility assessment was the Scandinavian multi-center trial, right?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Yes. That's what it says. They need to finalize that data.
MR. THOMAS: Wait a minute. He's asking you whether you know this, not what you're

Page 464

reading off the paper.
THE WITNESS: No, I'm reading it.
MR. THOMAS: Okay. Because if he's going to be a corporate representative, he's not prepared on this, and this is not part of his designation. So if you want to --
MR. THORNBURGH: He refers to -- part of the designation is the biocompatibility assessments. And he -- he just deferred to the clinical data available to support the non-cytotoxic effect or the self-limiting effect of the cytotoxicity in the TVT material.
So if that's a position he just took, then I ought to have an opportunity to cross-examine him on that issue.
MR. THOMAS: We've told you what he has prepared to talk about cytotoxicity. This goes well beyond it. I am not going to argue with you. You ask your questions, but --
BY MR. THORNBURGH:
Q. Before I do, are you aware of how much money -- strike that.
Are you aware that Dr. Ulmsten was the primary clinical researcher in the Scandinavian multi-center trial?

Page 465

MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: No, I do not know that.
BY MR. THORNBURGH:
Q. Do you know how much money -- what the financial interest was for Ulmsten, who was the inventor of TVT, that the results would be favorable?
MR. THOMAS: Object to the form of the question.
THE WITNESS: No, I do not.
MR. THOMAS: Scope.
BY MR. THORNBURGH:
Q. Do you know how much Ethicon was paid, or are you prepared to testify how much Ethicon paid to Ulmsten throughout the years for positive results in the Scandinavian multi-center trial?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: I have no knowledge of that information.
BY MR. THORNBURGH:
Q. I've just handed your counsel opposite an exhibit marked as 2254.

Page 466

MR. THORNBURGH: I have a copy for you, Counsel.
MR. THOMAS: This is the version that you've already highlighted?
MR. THORNBURGH: Yes, sir.
(Document marked for identification as Exhibit T-2254.)
MR. THOMAS: Did you say 2254?
Thank you.
BY MR. THORNBURGH:
Q. Have you seen this document before?
A. Yes.
Q. And this is a Prolene suture to which surface additives had been applied or evaluated to determine their tissue response characteristic in rat gluteal muscles at three, 14, and 28 days post implantation. Do you see that?
A. Yes.
Q. And the finding from this study is that two of the additives, Lubrol PX and Santonox R -- those are antioxidants, correct?
A. Yes.
Q. And those antioxidants, as you testified previously, can leach out of the Prolene mesh, correct?

Page 467

A. Yes.
Q. And this study found that two of the additives, Lubrol PX and Santonox R, elicit tissue responses significantly greater than controls. Do you see that?
A. Yes.
Q. Did Ethicon disclose in the 510(k) submission that the antioxidants that leach out of their mesh when tested against negative controls elicited a tissue response that was significantly greater?
MR. THOMAS: Object to the form of the question; scope.
BY MR. THORNBURGH:
Q. Doctor?
A. Let me just read the comments section.
Okay. This is an exploratory study where they coated the Prolene suture which already contains additives, but with additional additives on the surface.
Q. To mimic leaching, right?
A. No, to load up the suture with some components of the antioxidant package to see if there had been any impact on tissue reaction.

Page 468

Q. And the finding was that there was an impact on tissue reaction. There was, in fact, a significantly greater reaction in the controls, correct?
A. Yes, that's the case, but it's not relevant to Prolene suture or Prolene mesh, because the Prolene suture and Prolene mesh is not coated with additional additives like what was done in this experiment.
So it's an exploratory study to understand irritant potential of various antioxidants, but it has no relevance to current production products, the suture or mesh.
Q. Well, with all due respect, sir, the Lubrol and the Santonox R will leach out of the mesh fibers, correct?
A. It's possible that they will leach out of the mesh fibers. I think they do. As I've indicated, there's evidence for that.
At the same time, I've also indicated that in the 28-day Prolene mesh TVT mesh experiment, there was no increased evidence of tissue reaction indicating that if any of the additives were to leach away, it had no impact on the surrounding tissues.

Page 469

MR. THORNBURGH: Move to strike.
BY MR. THORNBURGH:
Q. We're going to discuss the 28-day study, but my question is: Was the Lubrol and the Santonox R -- will leach out of the mesh fibers, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. I've already admitted that these agents can leach out. This experiment is not relevant to that question.
BY MR. THORNBURGH:
Q. Well, this experiment does show that Lubrol and Santonox can elicit a greater tissue response, correct?
A. Only when smeared on the surface of a Prolene suture.
Q. Now, you talk about the 28-day study. Before we go there, I just have a couple questions for you about that, that I want to get my hands around.
The 28-day study that you are referring to is a study that compared Prolene flat mesh raw material to the TVT finished product, correct?

Page 470

A. As I recall, that was Prolene flat mesh finished goods, the final product, compared to TVT mesh, final product.
Q. Which would have also contained Santonox R and Procol and Lubrol, correct?
A. Yes.
Q. Okay. So you tested a mesh device that already had additives in it to another mesh device which already had additives in it, correct?
A. Yes, that's right, the difference being that the Prolene flat mesh is not cytotoxic in vitro, and the TVT mesh is cytotoxic in vitro.
Q. Now, I hear what you're saying, that there were studies done of the Prolene flat mesh, not the TVT, but the Prolene flat mesh used in hernia repair, that tested negative for cytotoxicity; is that what you're saying?
A. Yes. The same Prolene mesh that's in TVT mesh was negative.
Q. Was there a NAMSA Elution test done in that set of studies similar to the Elution test that was done in the TVT product which found moderate to severely -- severe cytotoxicity?
A. We'd have to look at the individual studies in the 510(k), and the summaries may be

Page 471

sufficient here, but I might need to go to the full study reports in the binders that we've brought. But let me take a look.

On ETH.MESH.00371569, there is a summary of the study that I am making reference to. In fact, two studies were conducted with the normal production Prolene flat mesh.

Q. And can you give me -- I don't have your binder.

MR. THOMAS: He's testified from your exhibit.

THE WITNESS: Yeah. It's your exhibit.

MR. THOMAS: It's the 510(k). 2105.

THE WITNESS: ETH.MESH.00371568.

BY MR. THORNBURGH:

Q. 15 --

A. 1568 and 1569. These were the cytotoxicity studies conducted with Prolene flat mesh. But one, an agarose overlay, was non-cytotoxic, as it was for the TVT flat mesh.

What you're referring to is the second study on Page 65 of that. That's ETH.MESH.00371569. This is a filter paper method, a

Page 472

little bit different than the ISO Elution method.

The ISO Elution method is taking an extract of the mesh and put it into contact with cells. In this case -- and it's a cytotoxicity assay that's commonly conducted for medical devices.

In this case, an extract is placed on a filter paper, which is then placed on an agarose overlay. And in that study, the test article was non-cytotoxic.

Q. That was a different method?

A. Slightly different. Slightly different, but very similar in that both used extracts, such that if there were leachables from the device, they would have gone into the extract and either the extract placed in contact with the cells or the extract pipetted onto filter paper put onto cells. Similar, but they're different.

MR. THORNBURGH: Move to strike, nonresponsive, after they're slightly different.

BY MR. THORNBURGH:

Q. I'll hand you what has been premarked as T-2132, which is a document draft entitled "Mechanisms Of Cytotoxicity In TVT Polypropylene Mesh."

Now, this is a discussion of the

Page 473

mechanisms of cytotoxicity and a summary of the tests that were performed by Ethicon, correct?

A. Yes.

Q. And this says that: As part of the overall assessment of biocompatibility of the TVT device, a number of cytotoxicity studies were conducted. Right?

A. Yes.

Q. And it goes on to say: After an evaluation of all the test results, only the polypropylene mesh component of the sterile TVT device was considered to be cytotoxic, and the severity was moderate to severe.

Do you see that?

A. Yes.

Q. In the ISO Elution testing using USP scoring system as slight, mild moderate, and severe.

Now, what does it mean to be moderately cytotoxic in terms of the number of cells that will die when they come into contact with the offending agent?

A. Yeah. I -- I know in -- I could pull up the study to find the detail.

MR. THOMAS: If you need to do that, do that. If you want that detail --

Page 474

THE WITNESS: Actually, let me get that detail. Let me look at a cytotoxicity study as an example.

BY MR. THORNBURGH:

Q. Well, just hold on a second. You don't know right now sitting here from your memory what the USP scoring system says concerning the number of cells that will die when they come into contact with the cytotoxic agent?

MR. THOMAS: Object to the form of the question. That's why he's prepared with all these notebooks, because he can't remember everything.

MR. THORNBURGH: Well --

MR. THOMAS: So if you want the answer to the question, he's going to consult the study.

MR. THORNBURGH: Number 4 on leaching.

MR. THOMAS: Do you want him to look at it?

BY MR. THORNBURGH:

Q. You're going to pull up some study. I'm asking what under the USP system, right?

It's greater than 50 percent of the

Page 475

cells, right?
MR. THOMAS: He'll check here and make sure.
THE WITNESS: For a moderate response, not more than 70 percent of the cells would be rounded and/or lysed, which would be evidence of cytotoxicity.
I should point out that a mild response, which is acceptable, results in not more than 50 percent of the cells having evidence of cytotoxicity.
BY MR. THORNBURGH:
Q. So at moderate cytotoxicity, up to 70 percent of the cells die that come into contact with the offending agent, correct?
A. Yes.
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. That's in accordance with the scheme. Not more than 70. So between 50 and 70.
BY MR. THORNBURGH:
Q. Okay. And for severe cytotoxicity, 70 to 100 percent of the cells that come into contact with the offending agent die, correct?

Page 476

A. Yes.
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. And under the testing conducted by NAMSA of the TVT finished product, between 50 and a hundred percent of the cells that came into contact died, right?
A. That's correct.
Q. Now, in your mechanism of -- this is your draft, right? This is your -- you wrote this; is that correct?
A. Yes, that's correct.
Q. And so you discuss -- who's M. Rippy?
A. She was a director of corporate product characterization at that time.
Q. Director of corporate product?
A. Corporate product characterization. That was the preclinical sciences group.
Q. Was there ever a final? Because I could only find the draft.
A. No, I don't have a final. I have not been able to locate a final signed copy.
Q. Did you ever provide or did Ethicon ever provide this document to the corporate product

Page 477

characterization person, Mr. or Mrs. Rippy?
A. If it was finalized, it would have gone to her, as well as the distribution on the page.
Q. That's what I'm -- I am trying to understand.
Do you know if this information was ever provided to the product characterization person, Mr. or Mrs. Rippy?
Is it Mr. or Mrs?
A. Marian.
I do not know that. A finalized copy has not been located.
Q. Do you know what her responsibility was as the corporate product characterization person at Ethicon?
A. She was the director of the group that included a biocompatibility surgical functionality, laboratory animal resources, product performance evaluation, and materials characterization.
Q. And that role is important in understanding the -- for future reference, understanding the safety and biocompatibility of Ethicon's products, correct?

Page 478

A. Yes. She was the leader of the group.
Q. Now, it says additional studies were conducted -- it goes on to say there was another -- it says: However, cytotoxicity of the testing of the polypropylene raw material also used in the manufacture of Prolene indicated that it was non-cytotoxic.
One thing we've established is that both of those -- both of those products contained Santonox and Lubrol, which we've seen are cytotoxic, or cause an increase in tissue response, correct?
A. The Santonox R was. And I think there may have been a change from Lubrol to Santonox R because of a change in supplier.
Q. I think there was a change in Lubrol to Procol. Right?
A. Well, no. I think the Procol LA-10 was a non-ionic surfactant. It was a processing aid, I believe.
And so it was the antioxidant, Santonox R and Procol LA-10 that had the most potential for in vitro cytotoxicity.
Q. All right. And you discuss -- you go on to discuss: Additional studies were conducted to

Page 479

better understand the nature of the cytotoxic potential of the polypropylene mesh under different conditions. Individual components of the polypropylene resin additive package used in the manufacture of the mesh were also evaluated to determine if any single additive might be contributing to the cytotoxic potential of the material.

Now, you say cytotoxic testing of the polypropylene mesh from this device was -- resulted in severe cytotoxicity.

Do you see that study, 196?

Hang on. Let me put it into context so that we're -- we look at this entire document.

Since there was the possibility of the use of localized high temperature during application of the heat shrink tubing might be contributing to the cytotoxicity of the polypropylene mesh, a study was conducted using low temperature heat shrink tubing to manufacture the TVT device.

And so you're able to rule out the use of the high shrink tubing as the cause for cytotoxicity, because when you used low temperature shrink tubing to manufacture the TVT device, the

Page 480

studies confirmed again that there was severe cytotoxicity in the polypropylene mesh, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Yeah. You would conclude that there was either no impact or the heat applied even to the low temperature heat shrink tubing was insufficient.

BY MR. THORNBURGH:

Q. Okay. Now, we know from two tests, that it's still the TVT mesh that is cytotoxic, right, not the process of the heat being applied to the heat shrink tubing, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: Well, there's still some heat to shrink a low temperature heat shrink tubing, but not as high as for a higher temperature heat shrink tubing.

So that's directional information, and it's -- the relevance, obviously, is that it's uncertain. There's still temperature added, but, apparently, it's sufficient to cause an in vitro cytotoxicity result.

BY MR. THORNBURGH:

Page 481

Q. Were you concerned that using a heat shrink tubing -- that that additional heat that's applied could cause the additives to leach to the surface of the Prolene mesh?

A. You would call that blooming. In the package, it would be a blooming of those additives of the surface, where in the body, it would be a leaching.

That was the -- that was the hypothesis at the time.

Q. And so even with the low and high tubing process, there's still heat being applied which could cause additives to bloom to the surface of the mesh, correct?

A. That's correct.

Q. And you go on to say: Cytotoxicity testing of the finished nonsterile TVT device resulted in slight cytotoxicity, which met USP acceptability criteria.

You go on to say: The material safety data sheet for the individual component of polypropylene resin additive package used to stabilize the polypropylene mesh were evaluated, and ISO Elution cytotoxicity testing was conducted for some of them, using maximum concentrations of these

Page 482

materials added to the resin, and then, if necessary, at the concentration of these chemicals which could be extracted from the polypropylene resin by water --

MR. THOMAS: By mesh.

BY MR. THORNBURGH:

Q. -- polypropylene mesh by water at 37 degrees Celsius for 24 hours to mimic the cytotoxicity extraction conditions. Right?

A. That's exactly right.

Q. All right. And you talk about another antioxidant, which is DLTDP, was tested and found to be non-cytotoxic, right?

A. Yes.

Q. And Santonox R, another antioxidant was tested 3 milligrams per milliliter and resulted in severe cytotoxicity, right?

A. Yes.

Q. And then you ran that test again with a lower volume of Santonox, which resulted from aqueous extraction of the polypropylene mesh, right?

A. Yes.

Q. And found no cytotoxicity when you lowered the level?

A. Yes. This would be a level to

Page 483

approximate what might come out after extracting the mesh in the manner for the original cytotoxicity work. So this would -- you would conclude here that Santonox R is not the element that is contributing to in vitro cytotoxicity.

Q. Santonox at .2 milligrams per milliliter was found to be non-cytotoxic, right?

A. Yes. Yes, that's correct.

Q. Santonox at 6 milligrams per milliliter was -- Santonox at 3 milligrams per milliliter was cytotoxic, right?

A. Yes, and probably as much as could be dissolved in water. It's relatively nonpolar. So this is the maximum amount that could be solubilized.

Then the second attempt was to approximate what might come out under actual extraction conditions, such that would occur as in a cytotoxicity study.

Q. And then you went on and tested Procol LA-10.

Do you understand that Procol and Lubrol are essentially the same antioxidant agent?

MR. THOMAS: Object to the form of the question.

Page 484

THE WITNESS: I didn't appreciate that, but...

BY MR. THORNBURGH:

Q. You don't know that?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: No. I know it as a Procol LA-10 here.

BY MR. THORNBURGH:

Q. Before you came here today -- before you came here today, had you seen this document authored by Dan Burkley dated February of 2003?

MR. THOMAS: May I have a copy of it, please?

MR. THORNBURGH: I'm sorry. We'll go ahead and mark it as an exhibit.

BY MR. THORNBURGH:

Q. It's been premarked as T-305.

Is this the first time that you've seen this document?

MR. THOMAS: Are you talking about the e-mail or --

MR. THORNBURGH: The e-mail and the document attached to it.

MR. THOMAS: Separate documents.

Page 485

BY MR. THORNBURGH:

Q. We'll probably look at the e-mail first, because attached is a copy of J. Karl's memo.

Who's J. Karl; do you know?

A. John Karl.

Q. And what was his position at Ethicon?

A. Polymer engineer.

Q. Okay. And J. Karl's memo indicating the R&D specifications for the various additives used in Prolene resin.

A. I've seen this.

Q. It says: If there is any biocompatibility and/or safety documentation for Prolene, it should have addressed the additives and made some worst case estimates.

Do you see that?

A. Yes.

Q. Then there was a memo attached from John Karl, an engineering fellow at Ethicon, who does an in-depth discussion of really the history of Prolene and the manufacturing process.

You've read this document before, right?

A. Yes, I've seen this.

MR. THOMAS: When you're talking

Page 486

about this document, you are talking about the e-mail and the memo?

MR. THORNBURGH: I am talking about the memo -- the memo attached, which is ETH.MESH.02268619, dated January 23, 2003 addressed to Dan -- Mr. Dan Burkley at Ethicon from a Mr. John Karl, engineering fellow from Ethicon.

BY MR. THORNBURGH:

Q. You've seen this before, right?

A. I've seen the memo you've pointed out. I don't believe I've seen the e-mail on the first page.

Q. Sure. It talks about how Ethicon had basically obtained the Prolene mesh from Montecatini Company. Did I pronounce that correctly?

A. I don't know. That was well before my time.

Q. Okay. It goes through, really, the in-depth background. We don't need to cover it all. But it does talk about how Prolene -- how Ethicon came to purchase Prolene from the original company, which was Montecatini, in it looks like New York -- it looks like the offices were in New York City.

He goes on and talks about their plant in West Virginia. And it goes on and talks

Page 487

about some of the changes in the company, of the polypropylene resin was still being sold to Ethicon from these various companies throughout the years.

A. Yeah. I think the original supplier was the Novo Mont plant, as I read this document. And they came from -- apparently, they bought the resources of Montecatini.

Q. It goes on to say: The objective to every polymer resin run has been to duplicate the original formulation as exactly possible, warts and all.

Do I read that correctly?

A. Yes.

Q. Do you know what warts Ethicon continued to include in their Prolene resin and manufacture of the TVT devices?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: No, although I think that knowing John, I think what he was saying was we're going to keep this original formulation as it is.

BY MR. THORNBURGH:

Q. No matter what bad things are associated with it, right?

Page 488

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: I can't put words in -- we have to think through where he's going with this. And that is -- and I've made this statement before. And that is we need to maintain the original formulation because we're accumulating a large database of preclinical and clinical experience that demonstrates the safety and functionality of this product.

BY MR. THORNBURGH:

Q. Long-term clinical data from folks like the Scandinavian folks, who were paid $400,000, as long as they -- the adverse events didn't change in their follow-up studies, correct?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Well, no. I was thinking of the beginnings of Prolene suture in 1965.

BY MR. THORNBURGH:

Q. In any case, they continued to manufacture the same Prolene resin, warts and all. No changes have ever been made in the chemistry with the exception of substituting Procol LA-10 for

Page 489

Lubrol and using the polypropylene form -- from a continuous reactor versus the original batch reactor.

Do you see that?

A. Yes.

Q. It says: We substituted Procol LA-10 for Lubrol solely because the Lubrol became no longer available. However, prior to consummating the substitution, we validated that the Procol was the same material as the Lubrol but from a different vendor.

Do you see that?

A. Yes. That's my understanding.

Q. Okay. So does that help you understand that the Lubrol and the Procol are really the same thing, just from a different vendor?

A. Okay. Thanks, Dan, for that clarification.

Q. Okay. And it goes on to say the added -- it goes on and lists the additives that were added.

It says: The additive package in use today is the same as was used in the original formulation from years ago with the two exceptions noted above.

Page 490

In addition, 1991, the Santonox levels were reduced slightly. Santonox is an antioxidant that protects the resin from thermal oxidation during extrusion.

So you see, actually, in 1991, after the ten-year dog study was started, that Santonox, an antioxidant, was actually reduced from the resin. Do you see that?

MR. THOMAS: Object to the form of the question.

THE WITNESS: I see the statement.

BY MR. THORNBURGH:

Q. So the -- the Prolene resin that was used in the ten-year study by Ethicon actually had less antioxidants in it than the sutures that are -- strike that.

According to this document, the history is correct. The Prolene sutures that were in the study conducted by Dan Burkley, the ten-year study, had more antioxidants than current production TVT, right?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: It says they were reduced slightly.

Page 491

BY MR. THORNBURGH:
Q. So there's less Santonox R in the Prolene polypropylene to protect against oxidation than existed prior to 1991, right?
MR. THOMAS: Object to the form of the question; scope. This is not a designation for him at all.
MR. THORNBURGH: Well, he was designated as the person to talk about degradation and degradation studies, so I think it's important for him to understand that --
MR. THOMAS: I am not going to argue with you.
MR. THORNBURGH: -- the ten-year data had more antioxidants in it than -- than the TVT mesh. Yet, it still showed surface degradation. Right?
MR. THOMAS: You're just not going to establish that through this witness. He's not been designated as a corporate representative on the chemical composition of the mesh.
MR. THORNBURGH: He has been designated for degradation. He's been designated as the person who will discuss --
MR. THOMAS: I'm not going to argue

Page 492

with you.
MR. THORNBURGH: -- the, you know, biocompatibility of this mesh.
BY MR. THORNBURGH:
Q. So according to this document, you'd have to agree it's based on this document and based on what you have seen, the ten-year study, that showed surface degradation in the Prolene sutures that were tested had greater antioxidants to protect against oxidation than current TVT?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. That's what this document would suggest, right?
MR. THOMAS: Excuse me. You've asked about three questions and haven't let him answer any of them. Do you want to start over again? Which question do you want him to answer?
Excuse me. Stop. Just --
BY MR. THORNBURGH:
Q. According to this document, the sutures that were tested by Dan Burkley in the ten-year data would have more antioxidants than the antioxidants in the TVT, correct?

Page 493

MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: This would indicate that.
It also indicates that when this minor change was made, the suture extrusion processes were fully validated to demonstrate that no adverse effect on the suture properties resulted from this change.
MR. THORNBURGH: Move to strike; nonresponsive.
BY MR. THORNBURGH:
Q. There wasn't even another question pending. You've got to wait for me to ask a question.
You were designated as the person regarding the additives and leaching, right?
MR. THOMAS: No.
BY MR. THORNBURGH:
Q. Leaching of additives, right?
MR. THOMAS: Leaching, period.
THE WITNESS: I understand that I am to address biocompatibility issues related to leachables, both in terms of local tissue reaction and any impact on cytotoxicity.

Page 494

BY MR. THORNBURGH:
Q. And this would indicate that one of the antioxidant additives, Santonox R, which -- do you have an understanding that Santonox R is used to prevent oxidation during the manufacturing of the Prolene meshes?
A. I've answered all that I can answer about this line of questioning. A polymer chemist -- need to be discussing these specifics with a polymer chemist or an engineer.
Q. Well, you rely on a lot of studies that were conducted prior to -- for your -- for your -- the studies related to degradation that predate 1991, which show that in 1991, there was a reduction of antioxidants in the Prolene suture, right?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: That's correct, and at the same time, there are plenty of studies conducted after 1991 that address these same endpoints.
MR. THORNBURGH: Move to strike everything after, that's correct.
We've got to change the tape.
THE VIDEOGRAPHER: We're now going

Page 495

off the video record. It's now 2:40.
This concludes Volume 2, Tape Number 3 of the videotape deposition of Dr. Thomas A. Barbolt.
(Short break.)
THE VIDEOGRAPHER: We're back on the video record. It's now 3:00 p.m.
This begins Tape Number 4, Volume 2 of the videotaped deposition of Dr. Thomas A. Barbolt.
BY MR. THORNBURGH:
Q. Okay. Dr. Barbolt, before we went off the record, we were talking about a change, a reduction in the levels of Santonox after 1991. Do you remember that?
A. Yes.
Q. And this document goes on to say that the Santonox is an antioxidant that protects the resin from thermal oxidation during extrusion.
According to this document, the Santonox is only there to protect against oxidation ex vivo, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I really can't address

Page 496

the intention of the inclusion of the Santonox R as an antioxidant, but, clearly, as it's stated, it helps prevent oxidation during extrusion from heat, but it may have other purposes to protect against any other oxidation. Since it's a free radical scavenger, that would be its function.
But short of that, this would be for a polymer engineer to address more specifically.
BY MR. THORNBURGH:
Q. Well, extrusion happens outside the body, right?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. During the manufacturing process?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Extrusion occurs during the manufacturing process.
BY MR. THORNBURGH:
Q. So according to this document, the Santonox is an antioxidant that protects the resin from thermal oxidation during the extrusion manufacture process, right?
MR. THOMAS: Object to the form of

Page 497

the question.
THE WITNESS: That's what it says.
BY MR. THORNBURGH:
Q. And we know from your prior testimony that the additives, including Santonox, Lubrol, DLTDP, those additives can bloom to the surface of the polypropylene sutures and meshes, correct?
A. Yes, they can.
Q. And can leach out of the -- out of the fibers in vivo, correct?
A. Yes. I think that's likely.
Q. It says calcium stearate is another additive; DLTDP, an antioxidant to improve long-term storage of the resin.
Do you see that?
A. Yes.
Q. So this is an antioxidant used, according to this document, used to prevent oxidation during the storage of the product, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I see that.
BY MR. THORNBURGH:
Q. Again, Santonox R is an antioxidant

Page 498

to promote stability during compounding and extrusion, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes. That's what it says.
BY MR. THORNBURGH:
Q. And Procol LA is a lubricant to help reduce tissue drag and promote tissue passage.
Do you see that?
A. Yes.
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. And the SCP pigment is a colorant to enhance visibility.
Do you see that?
MR. THOMAS: Same objection.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. So according to this document, the DLTDP and the Santonox are antioxidants used to prevent oxidation during either the manufacturing, compounding, or storage of the Prolene mesh, correct?

Page 499

MR. THOMAS: Object to the form of the question.
THE WITNESS: That's what's stated in this document.
BY MR. THORNBURGH:
Q. So let's go back to Exhibit T-2132.
Again, this document is the mechanism of cytotoxicity for TVT polypropylene mesh that we were discussing, which you drafted sometime while you were employed with Ethicon, correct?
A. Yes.
Q. And we discussed how Santonox R tested severely cytotoxic at 3 milligrams per milliliter, but non-cytotoxic at 2 milligrams per milliliter, right?
MR. THOMAS: Object to form.
It's .2 milligrams per milliliter.
MR. THORNBURGH: .2 milligrams per milliliter. Thank you, Counsel.
THE WITNESS: Yes, that's correct.
BY MR. THORNBURGH:
Q. And you go on to say that the Procol, which is the compound here, is the polyoxyethylene lauryl.
Do you see that?

Page 500

A. Yes.
Q. And the Procol was tested at 3.5 milligrams per milliliter and resulted in severe cytotoxicity.
Severe -- so then, you ran another test, reducing the volume of Procol, which again tested severely cytotoxic, correct?
A. Yes.
Q. And then you reduced it yet again. And the third test further confirmed the severe cytotoxic potential of Procol, correct?
A. Yes.
Q. And Procol is an additive that can bloom to the surface during the manufacturing process and leach out while implanted in a woman's body, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. It says: To evaluate the significance of the cytotoxicity in a clinically relevant in vivo system, an intramuscular implantation study was conducted in rats using cytotoxic polypropylene mesh from the TVT device and

Page 501

non-cytotoxic polypropylene mesh, Prolene.
The tissue reaction in TVT mesh was characterized generally by mild, chronic inflammation during the 28-day study, which was comparable to the tissue reaction observed for Prolene mesh.
Do you see that?
A. Yes.
Q. That was a short-term study, correct?
A. 28-day study. It would be considered short term.
Q. And that was a study that looked at inflammatory -- or tissue response differences between two mesh devices, both of which contained blooming and leaching additives, including Procol, correct?
A. Yes, but likely to different extents.
Q. You're comparing apples to apples -- apples to apples in this experiment, weren't you?
A. Apples to apples?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. Yeah.
A. I don't understand.

Page 502

Q. Well, we've already -- you've already established, and these documents establish and your testing established, that Procol, which was contained in both of these products, was severely cytotoxic, even at very low levels, right?
A. Yes, as we discuss in the paragraph at the top.
Q. So you are testing two mesh products, both of which contained a severely cytotoxic additive, to compare the difference in tissue reaction, correct?
A. Yes.
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. Now, one of the differences I assume that you'll testify to is -- well, strike that.
In summary, this data suggests that the probable mechanism of cytotoxicity of the polypropylene mesh from the TVT devices is the presence of Procol LA-10, a potent non-ionic surfactant, with the ability to disrupt cell membranes and cause cell death in in vitro systems. Right?
A. That's correct.

Q. The increased cytotoxicity of polypropylene suture -- and this is a question I have for you.

The increased cytotoxicity of polypropylene suture after autoclaving can be attributed to the increased amount of Procol LA in aqueous extracts. Thus, any treatment in polypropylene mesh which would result in more or less of Procol LA-10 available for extraction would be expected to result in greater or lesser cytotoxicity respectively.

Do you know if the polypropylene in TVT is autoclaved?

A. No. Sterilized by ethylene oxide.

Q. Okay. But the issue with autoclaving was the additional heat that is applied to sterilize the mesh, right?

A. The suture and -- yes, that's correct.

Q. Which can cause blooming of these additives at the surface of the polypropylene. Is that correct?

A. Yes. That's the hypothesis.

Q. Now, what we know from your prior testimony is that the TVT device undergoes the heat

shrink tubing, which also can cause blooming of antioxidants like -- or the additives like Procol to the surface of the TVT fibers, correct?

A. Yes, that's correct.

Q. And if the Procol blooms to the surface during the manufacturing process, it can increase the risk of cytotoxicity, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: It can increase the risk of cytotoxicity in vitro. However, all of the in vivo implantation studies suggest that that's not the case; that the substance that might cause severe in vitro cytotoxicity is not making a contribution to increased tissue reaction in vivo.

BY MR. THORNBURGH:

Q. Well, some of the things that -- some of the symptoms that we would see if polypropylene in TVT is cytotoxic would be increased tissue reaction, wound healing defects, and ulcerations, correct?

A. I think certainly increased tissue reaction and adverse impact in wound healing. The ulceration question, it kind of depends. I generalized by saying that.

Q. Do you recall writing a biocompatibility assessment where you say specifically that the -- what you'd expect to see in vivo if TVT was cytotoxic would be delayed or wound healing defects or ulcerations?

A. I don't recall that specifically. Certainly, the adverse impact in wound healing. And I guess if it's severe enough, it might cause ulceration of overlying tissue, but I don't recall that specifically.

Q. You would agree that based on the evidence, TVT, the Prolene in TVT, showed evidence of cytotoxicity --

MR. THOMAS: Object to the form of the question.

BY MR. THORNBURGH:

Q. -- at least in vitro?

A. Yes. It showed evidence of cytotoxicity in vitro.

Q. And nowhere in the IFU are those findings disclosed to physicians, correct?

A. Yes. And that's because there's no translation to increase tissue reaction or adverse impact in wound healing.

Q. Have you seen the studies that show

that the Prolene mesh can cause chronic wound healing problems?

MR. THOMAS: Object to the form of the question.

THE WITNESS: No. I'd have to see the specific reports that you're talking about.

BY MR. THORNBURGH:

Q. I am asking you: Do you recall seeing any studies as you sit here -- did you review any studies before you came in here today that showed that the Prolene -- that the polypropylene meshes can lead to chronic wound healing problems?

MR. THOMAS: Object to the form of the question.

THE WITNESS: No.

BY MR. THORNBURGH:

Q. Did you review any studies before you came here today that show that the Prolene in TVT can cause erosions and extrusions through the vaginal wall?

MR. THOMAS: Object to the form of the question.

THE WITNESS: No. And that would be in the clinical area, and my responsibility here is to address preclinical questions.

Page 507

BY MR. THORNBURGH:
Q. Did you look at any -- any of the explant reports that Ethicon received that showed that women who had mesh devices explanted, also, some of those women had ulcerations?
MR. THOMAS: Object to the form of the question.
THE WITNESS: There would be a clinical explant, and I have not reviewed any of that information.
BY MR. THORNBURGH:
Q. You have also been designated as the 30(b)(6) witness to discuss the specifics of all testing related to TVT products during the design, development stages, including but not limited to porosity testing, particle loss, degradation, and leaching. We'll shorten that up.
You have also been designated as the Ethicon person who will testify regarding all testing related to the TVT products and particle loss. Correct?
A. Yes, that's correct.
MR. THORNBURGH: Off the record.
THE VIDEOGRAPHER: Off the video record, 3:18.

Page 508

(Short break.)
THE VIDEOGRAPHER: Back on the video record, 3:24.
BY MR. THORNBURGH:
Q. Doctor, I want to mark as -- give me one second.
There we go. I am going to mark as Exhibit Number 2255 an e-mail dated February 27, 2004.
(Document marked for identification as Exhibit T-2255.)
BY MR. THORNBURGH:
Q. This is an e-mail from Dan Smith to a number of -- or to Janice Burns dated February 27, 2004, discussing issues with TVT and particle loss. Right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I've not seen this memo, and I am not sure that it relates to the biocompatibility or particle loss in a preclinical arena. I have to read through here --
MR. THOMAS: I think they showed it to you at your last deposition.
MR. THORNBURGH: Yeah.

Page 509

THE WITNESS: Okay.
BY MR. THORNBURGH:
Q. And it will relate preclinically.
A. Okay. Fine.
Q. We'll talk about it and refresh in the preclinical context.
A. Okay. Fine.
Q. Now, this is a document that discusses problems with particle loss that were being experienced -- were experienced by Ethicon regarding its TVT products, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I'm sorry. I was kind of reading through here, and I see that I have looked at it before.
Could you please repeat that question?
BY MR. THORNBURGH:
Q. Yeah. This is an e-mail from Dan Smith to Janice Burns which discusses problems of particle loss that were being seen by doctors in the field who were using the TVT product, right?
MR. THOMAS: Object to the form of the question.

Page 510

THE WITNESS: Yes. That's what it looks like.
BY MR. THORNBURGH:
Q. And in that context, Dan Smith says: This is not going away any time soon, and competition will have a field day. Major damage control offensive needs to start to educate reps and surgeons upfront they -- that they will see blue shit, and it is okay. This is why I wanted to launch TVT-O in clear.
Do you see that?
A. Yes.
Q. And when you worked for -- as Ethicon, you recognize that there is -- at least during the mechanical cut days of TVT mesh, there was a problem with particles falling away from the mesh, right?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. In fact, that same month -- I've handed you what's been marked as Exhibit Number 2256.
(Document marked for identification

as Exhibit T-2256.)
MR. THOMAS: May I have one, please?
BY MR. THORNBURGH:
Q. That same year, in November of 2004, Ethicon received an e-mail concerning complaints from Dr. Eberhard.
It says: Dear all, please see attached below a letter with pictures of competitor's device and its translation from Dr. Eberhard, an important customer in Switzerland, regarding mesh fraying. Regarding the mesh frayed complaints, decision is not open corrective action -- a decision to not open corrective action is based on the following memo. Could you please give feedback?
So this is an e-mail regarding Dr. Eberhard, who had written a letter to Ethicon regarding problems with the mesh devices, right?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Yes. It looks that to be the case.
BY MR. THORNBURGH:
Q. And David Menneret on November 9th -- of November 12th of 2004 wrote that: We already

received similar complaints. This kind of issue is usually attributed to over-tensioning of the tape during the procedure. Fraying is inherent in the product based on the mesh construction. When any amount of tension is applied to the mesh, fraying occurs. Stretching of the mesh increases the probability of fraying.
Do you see that there?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. I am going to put it in the scope of the deposition. So according to David Menneret, one of the problems with fraying and particle loss was from tensioning of the mesh and specifically tensioning of the TVT tape or the tape that was being used by Ethicon, correct?
MR. THOMAS: Same objection.
THE WITNESS: Yes. I think that's what they're referring to.
(Whereupon, a discussion was held off the record.)
(Document marked for identification as Exhibit T-2257.)

BY MR. THORNBURGH:
Q. What's been marked as Exhibit Number 2257 is a document or a fax that was received by Basso Sibylle to David Menneret, who said: Attached is Dr. Eberhard's letter regarding TVT blue tape.
Do you see that?
A. Yes.
(Document marked for identification as Exhibit T-2258.)
BY MR. THORNBURGH:
Q. I've marked as Exhibit Number 2258 the translated letter from Dr. Eberhard, who writes: Dear Emilie, Business Unit Manager Gynecare Switzerland. Please find attached a TVT tape which was used as a demo unit for patients before they had their operation. Already at the operation, it is embarrassing to see how the tape is crumbling. It gets worse if there is stretch on the tape.
I can't understand that no one will solve the problem for such a long time. At least as the tape has becoming blue, everyone has realized that the quality of the tape is terrible. A tape has to be weaved and should not crumble. Please try one and you will see that the tape is crumbling.

Did I read that correctly?
MR. THOMAS: Object to the form; scope.
THE WITNESS: Yes.
(Document marked for identification as Exhibit T-2259.)
BY MR. THORNBURGH:
Q. Marked as Exhibit Number 2259 a compilation of e-mails --
MR. THOMAS: May I have one, please?
MR. THORNBURGH: I'm sorry, Counsel.
BY MR. THORNBURGH:
Q. -- a string of e-mails in which Charlotte Owens was one of the recipients and authors of the e-mails.
Do you know who Charlotte Owens is?
A. I think we overlapped a little bit. Obviously, she is a medical director of Gynecare.
Q. So she was in charge, the director of the medical affairs part of Ethicon, right?
A. Yes, for Gynecare.
Q. For Gynecare.
And she received, according to this document, an e-mail from Dan Smith, who appears to have included an e-mail or an excerpt from something

authored by Steve Bell of Gynecare.
It says: Dear all, as more and more customers now move to TVT blue and TVT-O with blue mesh, you may sometimes hear, I can see small blue pieces come off the mesh. What's wrong?
The key points, it says, number two, the same -- number one, Gynecare blue TVT mesh and Gynecare clear TVT mesh are exactly the same.
Number two, the same number of particles came off the clear mesh when it was stretched.
Do you see where it says "when it was stretched"? Do you see that?
A. Yes.
Q. Okay. It's just that you see them against the tissue and skin more when they are blue. This is no different to what has happened in the past seven years with TVT.
Reassure your doctors that this is part of the success of TVT. The way we have cut the mesh makes the edges softer, and we feel that this has been a crucial success factor in TVT. Reassure that Prolene has proven to be inert.
Do you see that? "Proven to be inert." Right?

A. Yes, I see that.
Q. In summary, be proactive. The competition will try to target this, especially Bard, as they have a sealed edge tape, and remind your customers it is the same as clear. It is proven safe implant. In the blue format over 100,000 have been implanted worldwide. Remind them that the benefits -- of the benefits of blue mesh. Remind them it is inert Prolene with over 25 years of health. Remind them our wealth of clinical data with ultra low complication rates.
Do you see that?
A. Yes. I can read it.
Q. Okay. So number one is -- there's particle loss being seen when the tape is stretched. Do you see that?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Yes, I see it.
BY MR. THORNBURGH:
Q. Okay. And, number two, we know from what we've seen in the internal studies by Ethicon that the Prolene in the TVT mesh is susceptible to surface degradation, correct?
MR. THOMAS: Object to the form of

the question.
BY MR. THORNBURGH:
Q. Yes, Doctor?
A. Yes.
Q. This doesn't -- this summary doesn't say remind physicians that Prolene mesh is susceptible to surface degradation, does it?
A. I don't know that I should be even commenting on this exchange between a marketing person and the field.
Q. Well --
A. First, he's not a scientist. Second, I am not sure what it's got to do with the preclinical data that we brought here to talk about.
Q. I am going to put it all into context. I assure you.
A. Okay.
Q. But it says -- it doesn't say remind physicians who are purchasing these permanent implants which are going to be put into -- in and around the vaginal area of the woman's body, that the surface area or the surface layer of the Prolene in the TVT is susceptible to surface cracking or surface degradation, right?
MR. THOMAS: Object to the form of

the question. Scope.
THE WITNESS: I want to make a distinction between particles shed from the mesh, which I consider a macroparticle, and the kind of microparticles that you're alluding might shed from or as a result of some sort of surface cracking observed on the Prolene fiber. Two different issues.
BY MR. THORNBURGH:
Q. Both --
MR. THOMAS: Are you finished?
THE WITNESS: Yeah.
MR. THOMAS: Sorry.
BY MR. THORNBURGH:
Q. Both of which, by themselves, can elicit a -- an inflammatory response.
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. In fact, nanoparticles or microparticles will excite macrophages more than macroparticles will.
MR. THOMAS: Which question do you want him to answer?
BY MR. THORNBURGH:

Page 519

Q. Correct?
MR. THOMAS: Which question do you want him to answer? You posed two of them.
MR. THORNBURGH: Both.
MR. THOMAS: One at a time.
MR. THORNBURGH: My last one first.
THE WITNESS: So the first part, the fragments that we've talked about that have been observed alongside the suture and in what I call macroparticles have a tissue reaction to them very similar to the polypropylene fiber.
And the second question in terms of these microparticles that I make reference to that you allude would come off the surface as a result of surface cracking, there's been no evidence in any of the 49 documents that I've brought today that there's an increase in tissue reaction over time. And, in fact, in many studies, there's a diminution of the tissue reaction over time. So there's no evidence to support that second piece.
BY MR. THORNBURGH:
Q. The truth is the testing that you and Ethicon were doing preclinically was really marketing studies. They were studies to -- that were being conducted because of the threat from

Page 520

competitors like Bard.
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Absolutely not. The preclinical studies conducted by Ethicon were either for regulatory submission or for internal information to advance product development.
BY MR. THORNBURGH:
Q. When you did rabbit studies that looked at particle loss in rabbits, the tape that was being implanted in the rabbits was not undergoing the same type of stresses and strains that the tape undergoes in the human environment or the human condition when the device is being implanted, correct?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: As I recall in that study -- and we could make reference to it, and I probably should go to it -- that they implanted the mesh in a manner that the mesh might be implanted in patients; that is, insertion, passage through muscle, which would offer up some tension, and then implantation.
BY MR. THORNBURGH:

Page 521

Q. It's not the same implant condition that is occurring in women who are having these implants put in their bodies for the rest of their lives --
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. -- right?
MR. THOMAS: Scope.
THE WITNESS: I don't know all the parameters of that condition that you make reference to, okay, because I suspect that each patient has different issues.
And this study was an attempt to make the implantation procedure very consistent so that we could determine whether or not there is stretching of the tape or deposition of particles in the surrounding tissue.
BY MR. THORNBURGH:
Q. You didn't answer my question completely.
It's not the same implant condition that is occurring in women who are having these implants put into their bodies for the rest of their lives.

Page 522

MR. THOMAS: Object to the form of the question; scope. And, also, he did answer your question.
BY MR. THORNBURGH:
Q. Well, number one, rabbits are quadrupeds, not bipedal, right?
A. Well, I thought we were talking about the conditions of implantation, and it would have nothing to do with the number of legs.
Q. Well, we're talking about -- we're talking about the condition, the real human condition, compared to the animal condition where you conducted these studies.
MR. THOMAS: He's not a clinical guy.
MR. THORNBURGH: Number one -- I think he can say pretty easily that rabbits are bipedal -- or quadrupeds, not bipeds.
BY MR. THORNBURGH:
Q. Right?
A. I said I don't know all the conditions in the clinical situation that you're alluding to and whether or not they would compare with the passage of mesh through skeletal muscle of rabbit.
Q. Your rat study, which has previously

Page 523

been marked as T-2133, ETH.MESH.05316775 --
MR. THOMAS: Which one are we talking about, Dan?
MR. THORNBURGH: Sorry.
MR. THOMAS: Which study?
MR. THORNBURGH: Yeah. The histological evaluation and comparison of mechanical pullout strength of Prolene and Prolene Soft mesh in a rabbit model.
Let's go ahead and mark it as an exhibit.
It's already been marked, Exhibit Number 2133. Sorry. 2133. It was marked at a prior deposition.
MR. THOMAS: Oh, okay.
Do you have another one?
MR. THORNBURGH: Yeah, I do. Sorry. I think I left the extra copy -- oh, found it.
2133.
BY MR. THORNBURGH:
Q. Now, Ethicon was concerned about the -- what the competition would say about the TVT products as a result of the particles that were being seen with the TVT blue, correct?
MR. THOMAS: Object to the form of

Page 524

the question; scope.
THE WITNESS: Yeah. And I guess I can't really address what Ethicon was thinking and why they did stuff, only to -- insofar as it reflects the documents that we brought here today to talk about biocompatibility or any preclinical studies.
BY MR. THORNBURGH:
Q. So you conducted a 14-day rabbit study, right?
A. Ethicon conducted such a study.
Q. And women who have these devices implanted in their bodies are -- the intention is that these implants will remain in their bodies for the rest of the woman's life, correct?
A. Yes.
Q. Now, how much mesh -- what was the size of the mesh implanted in the rabbits?
A. The mesh was -- the TVT tape width, about 10 millimeters. That's what was implanted. And samples of Prolene Soft mesh and ultrasonically cut mesh were done in a very similar way.
And as I look on Page ETH.MESH.05316780, the intention was to leave 3 centimeters of that mesh within the epaxial

Page 525

musculature.
Q. Okay. And how much mesh is implanted in women during the implant process?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: I don't know that number. That's a clinical issue, and it would depend on which TVT product you're talking about.
BY MR. THORNBURGH:
Q. Well, the more mesh, the more particles there are to flake off of the mesh device, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I don't know that for certain.
BY MR. THORNBURGH:
Q. You don't know that?
A. No.
Q. Did you look at the Pariente study before you came here today?
A. No.
Q. Do you recall discussing the Pariente study during your deposition last time?
A. The name sounds familiar.

Page 526

Q. Do you recall that in the Pariente study, it was found that 8.5 percent of the particles in the TVT mesh fell away from the TVT product?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: I don't recall that information.
BY MR. THORNBURGH:
Q. Did any of your studies try to mimic the stresses and strains that were used in the Pariente study during the implantation of the mesh in rabbits, and in this case, in rabbits for 14 days?
MR. THOMAS: Object to the form of the question; scope.
Do you have one to show him?
THE WITNESS: Was it a clinical study or a preclinical study?
MR. THOMAS: That's why I want you to see it.
MR. THORNBURGH: It was an ex vivo study.
THE WITNESS: It could be ex vivo from animals or humans.

Page 527

BY MR. THORNBURGH:
Q. Do you know sitting here today whether the studies that you did were -- whether or not you used the Pariente study to determine particle loss in any of the studies that you did?
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: It's not indicated in the study report, any reference to the Pariente study.
BY MR. THORNBURGH:
Q. What loads were used when implanting the 3-centimeter by 1-centimeter samples in these rabbits?
MR. THOMAS: Object to the form of the question.
THE WITNESS: As indicated in the study report, the mesh was drawn through the epitaxial musculature, and whatever forces that would offer the mesh, that's what happened.
BY MR. THORNBURGH:
Q. And can you hold up for the ladies and gentlemen of the jury approximately 3 centimeters?
A. Maybe an inch and-a-half.

Page 528

Q. So your study in rabbits was about an inch and-a-half piece of mesh that was implanted in the muscle of the rabbit for 14 days max, right?
A. That's correct.
Q. Did you measure the force by Newtons or the load by Newtons that would be used or was used during the implantation process to determine whether or not it would mimic the implantation conditions in human women?
A. No assessments of force required to implant the mesh samples was recorded, only the explant tensions.
Q. Do you know what forces are used during the implantation process in women?
MR. THOMAS: Object to the form of the question. Scope.
THE WITNESS: It is a clinical question.
BY MR. THORNBURGH:
Q. Well, isn't that -- isn't that clinical information important when you're trying to determine particle loss in rabbits?
A. This preclinical study was an attempt to simulate implantation in patients. And it is what it is.

Page 529

Q. Well, then, you didn't consider the level of force used when implanting a TVT-Retropubic in women to try to mimic the same loads being applied to the one and-a-half inch piece of mesh that you're implanting in these rabbits, did you?
A. I can't speak to anything that was done in the clinical environment.
Q. Did you ask anybody from the clinical environment: Hey, you know what? We want to try to, in the preclinical environment, to test this issue. We want to determine the amount of force or loads that are being applied during the implantation of a larger piece of mesh in women so that we can mimic that condition in the preclinical studies that we're doing with one and-a-half piece of mesh?
A. That was not done --
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. You did not. Did you have any discussions with anybody in the clinical arena to determine the implant conditions in women to try to mimic those implant conditions in the animals that you were testing this mesh in?
A. That's not indicated in this report.

Page 530

Those discussions may have taken place.
Q. Did you do that? Did you try -- did you understand or try to understand the amount of force or loads in any of the studies that you did in -- that were -- that were needed for implantation in women so that you could mimic the same implant condition in your preclinical studies?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Again, you're talking about data that would be collected in a clinical environment, and I am not here to address that other than the preclinical data that we brought and anything that's relevant to it.
BY MR. THORNBURGH:
Q. Did you discuss with anybody for any of the preclinical studies or before you walked in here today what the implant conditions are like in terms of a force required to implant the stretching that's done during the implant procedure so that you could gain a better understanding of your preclinical studies?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That's the kind of

Page 531

information that would be in the clinical arena, and that's not part of what I am here to discuss.
BY MR. THORNBURGH:
Q. But you didn't discuss with anybody in the clinical arena whether or not the preclinical studies that you're trying to rely on now were done in a condition that would mimic the human implant condition?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I think I've answered that three times, and the same answer I'll give now, and that is this information would be collected in a clinical environment and is not part of what I am here to discuss.
BY MR. THORNBURGH:
Q. Let's go ahead and mark as Exhibit 2260 the Pariente study.
(Document marked for identification as Exhibit T-2260.)
MR. THORNBURGH: Dave, I have a copy for you, and I just don't have -- it's not stapled.
MR. THOMAS: That's fine. Thank you.
BY MR. THORNBURGH:
Q. You've seen this study before,

Page 532

haven't you?
A. I think I have, but it doesn't look so familiar. The name does seem familiar, but I'd have to read through it to see what happened here.
Q. Do you want to take a moment and look at it?
A. Sure.
Okay. This looks like an in vitro study.
Q. Did you look at this study before you came in here today?
A. No.
Q. You don't recall looking at the study with me during your prior deposition?
A. Again, I think the name rings a bell, but I've looked at a lot of studies.
Q. Okay. Well, in the Pariente study, the investigators were looking at -- as their endpoint or one of their endpoints, particle loss, correct?
A. Yes.
Yes, I recall the study now. This one we discussed during the last deposition.
Q. And it says here: To evaluate the shedding of particles, each sample was weighed

Page 533

before and after soft procedure, and values range from 0 to 8.5 percent of initial weight.
Did you -- in any of your studies, did you weigh the sample pre and post procedure?
A. No.
MR. THOMAS: Pre-implant?
BY MR. THORNBURGH:
Q. Pre-implant and post explant.
A. No. That would not be practical, because there would be tissue adherent to the mesh, and it would alter its weight.
Q. So you didn't look at the weight to determine particle loss, did you?
A. No. But we looked at something more important than that in the study that we discussed earlier, and that is whether or not particles were observed in the immediate vicinity of the implant.
Q. You didn't look at weight, did you?
A. No.
Q. You didn't determine the percent of particle loss in any of your studies, did you?
A. As I pointed out --
Q. It's a yes or no question.
A. As I pointed out, weighing a mesh after implantation would not be useful, because

Page 534

there would be additional weight of tissue adherent to it.
Q. It could dissolve the tissue, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That would be a possibility.
BY MR. THORNBURGH:
Q. So you could have weighed it after dissolution or dissolving -- desiccation of the tissue, right?
A. That's possible. That could introduce other things that you would have to control for, but, clearly, there's no end to the number of studies that could be conducted.
Q. But you didn't do that study, did you?
A. No.
Q. And you didn't determine the percentage of particle loss, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That's correct.
BY MR. THORNBURGH:
Q. The study goes on to say: During

Page 535

surgical use, these articles are released in soft tissue, and it is not possible to know where they go.

MR. THOMAS: There's no question pending.

BY MR. THORNBURGH:

Q. Do you see that?

A. Yeah, I see it.

Q. And that's true? When particles are released into soft tissue, they can migrate, can't they?

MR. THOMAS: Object to the form of the question.

THE WITNESS: That's not very likely. With any particles, any macroparticles that would be adherent to the mesh or they might flake off the mesh in vivo, they would reside in the immediate vicinity of the implant, and they would be surrounded by connective tissue, just like each element of the mesh.

BY MR. THORNBURGH:

Q. When I get a splinter in my finger, no matter how deep it is, my body's -- my body's inflammatory response to that little tiny piece of splinter will push that splinter out of my body,

Page 536

migrate it from where it found itself initially until it's outside of my body, won't it? That happens, doesn't it?

A. That can happen if it's close enough to the surface of your skin.

Q. So migration of particles is possible as a result of the inflammatory process that's taking place in the human body, right?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Highly unlikely.

BY MR. THORNBURGH:

Q. And that's based on what, sir?

A. My experience looking at implanted materials and the experience from the Prolene suture NDA, which calls out macroparticles of the suture, likely resulting from a swaging process of macroparticles that got adhered to the suture, and they got implanted inadvertently with the suture.

And what's observed is that there's a tissue reaction around the filament of the suture and then adjacent to it, the particle, or the very similar reaction around it.

There's no evidence that that particle will migrate away from the fiber from which

Page 537

it might be associated with.

Q. During surgical use, these particles are released in soft tissue, and it is not possible to know where they go.

That's what these authors write, correct?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: That is the opinion of these authors.

BY MR. THORNBURGH:

Q. When these authors tested particle loss, they found that the TVT lost the most particles of all the things that were tested, correct?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Under the conditions of their testing, that's the case.

BY MR. THORNBURGH:

Q. And they found that TVT lost 8.5 percent of the particles, right?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: I think -- I think they

Page 538

mean 8.5 percent of the weight was lost as particulates.

BY MR. THORNBURGH:

Q. Yeah. I'm sorry. They found that 8.5 percent of the weight of the TVT sling was lost to particles, correct?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: I think that's what they're saying.

BY MR. THORNBURGH:

Q. Almost 10 percent of the TVT sling was lost in their study through particle loss, right?

MR. THOMAS: Object to the form of the question; scope.

THE WITNESS: Eight and-a-half percent.

BY MR. THORNBURGH:

Q. Now, what loads were used to test TVT particle loss?

MR. THOMAS: In what context, Dan?

MR. THORNBURGH: In this study.

MR. THOMAS: In which study?

MR. THORNBURGH: The Pariente study.

MR. THOMAS: Thank you.
BY MR. THORNBURGH:
Q. Measured in K per Newton. Do you know what that means? Peak load?
A. Well, I'm just looking at the text where they talk about a soft procedure, and I'm looking for the data that would be corresponding to it.
Q. I think if you look here, maybe this might help.
Do you see Table 1?
It shows low deformation curves?
A. No. It looks like they gave each material a different load.
Q. Starting at?
A. TVT at .041 ranging to .012 for I-Stop.
Q. Do you know how much load is used in the implantation of the TVT?
A. I do not.
Q. Do you know how much load you used when you implanted the 1.5 by -- 3-centimeter by 1-centimeter piece of mesh in the rabbits use study?
A. That was not measured.
Q. You don't know sitting here today if

the loads that you used would have mimicked the loads used during the implantation of TVT in an actual woman, right?
A. Well, as I mentioned four times previously, that would be data coming from the original -- the clinical arena, clinical environment, and it's not what I am here to address.
Q. And that information wasn't important for you when you designed the studies that looked at particle loss, was it?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Obviously, it was not considered necessary to execute this protocol.
BY MR. THORNBURGH:
Q. You would agree that if 8.5 percent of particles are being lost during the implant procedure on the TVT mesh, that that would increase the inflammatory response.
MR. THOMAS: Object to the form of the question; scope.
THE WITNESS: Highly unlikely, given the mass of material implanted as part of a tape.
Think about all of the monofilaments woven into a mesh, and think about some particulates

lying adjacent to the implant. It would have the same kind of tissue reaction. It would be probably not discernable against the background of implantation of a mesh, even if it had no particles.
(Document marked for identification as Exhibit T-2261.)
BY MR. THORNBURGH:
Q. I marked as Exhibit Number 2261 a side-by-side photograph of the -- a document that includes a side-by-side photograph of mechanical cut TVT mesh and laser cut TVT mesh.
Have you seen this before?
A. I don't think so.
Q. Do you see where it says side-by-side relaxed after 50 percent elongation?
MCM would mean mechanical cut mesh, right?
A. Yes.
MR. THOMAS: Object to the form of the question; scope.
All of this is beyond -- excuse me. All of this is beyond what he's been designated for.
MR. THORNBURGH: No, it's not.
BY MR. THORNBURGH:
Q. LCM is laser cut mesh? Do you see

that?
Do you see that?
A. I understand it's outside my area.
Q. What -- what? No, it's not. I am going to put it in context.
What percentage of elongation was used in any of your studies to determine particle loss?
Did you ever measure the elongation that was being applied during the implantation of this device in any of the preclinical studies that you conducted?
A. This might be the sixth time that I've responded to that question, and it's the same.
This is data that would be acquired in the clinical environment and is not part of the preclinical database that I'm here to discuss.
Q. No. I asked you a different question. My question was: In any of the preclinical studies that you did or that Ethicon did to look at particle loss and tissue reaction, did you ever look at or record the percentage of elongation during the implantation in the animal study?
A. Not that I'm aware of.

Page 543

Q. Do you see where it says degradation?
MR. THOMAS: Where? What page are you on?
MR. THORNBURGH: I'm on the side-by-side image of the MCM versus LCM.
BY MR. THORNBURGH:
Q. You were designated as somebody that would talk about evidence and studies regarding degradation, right?
MR. THOMAS: We provided the studies on which he's prepared to testify. This is not one of the documents.
MR. THORNBURGH: You only provided studies that would support your position, not studies that would show that your position was incorrect.
MR. THOMAS: Now, we invited you to ask him to review other things you wanted to be prepared on, and you didn't. So this is -- if you want him to be prepared on it, he'll study it and come back with an appropriate answer. He's not prepared on it today.
BY MR. THORNBURGH:
Q. Do you see where it says degradation, Doctor?

Page 544

A. I am not prepared to respond to those questions today. It is not part of the preclinical data package that I put together to address degradation questions.
Q. You see where it shows the particles that were lost? Do you see that? Do you see all those flakes?
A. I can see particles in the photograph.
Q. You're not suggesting to the ladies and gentlemen of the jury that there won't be an individual inflammatory response to each one of those particles in tissue?
A. It would pale by comparison to the tissue reaction from the implanted tape.
Q. But there will be an increased inflammatory response or an inflammatory response to the individual particle, correct?
A. There will be an inflammatory response to that individual particle, but it will not be appreciated against the inflammatory response of the entire case.
Q. The phagocytes will try to gobble up that foreign body, won't they?
A. One will not be able to differentiate

Page 545

contribution of a particle to the overall reaction to the entire tape.
Q. Inflammatory cells would be released to attack that particle, to try to rid the body or the animal of those particles, correct?
A. The tissue reaction to these particles would be no different to the tissue reaction to any filament in any part of the mesh.
Q. But there will be a tissue reaction, right?
A. Yes.
Q. And when you increase the surface area of a foreign body, that will increase the body's inflammatory response, won't it, sir?
A. Any increase in tissue reaction will not be perceptible against the background of tissue reactions of the implanted tape.
Q. When you increase the surface area, you increase the inflammatory response. Right, Doctor?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That's a general -- that's a general principle.
BY MR. THORNBURGH:

Page 546

Q. And the principle is true. The principle -- the answer to that principle would be yes. When you increase the surface area, you increase the inflammatory response.
A. Not in this case.
Q. In all other cases except for cases against Ethicon products?
MR. THOMAS: Object to the form of the question.
THE WITNESS: In any case where the addition of particles -- in any case where the addition of the inflammatory reaction to a particle could be perceived against a tissue reaction of the implanted tape itself would be insignificant and unappreciable.
BY MR. THORNBURGH:
Q. General scientific principle is when you increase the surface area, you increase the inflammatory response, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That's a general scientific principle.
MR. THORNBURGH: Off the record for a minute.

Page 547

THE VIDEOGRAPHER: Off the video record, 4:14.
(Short break.)
THE VIDEOGRAPHER: Back on the video record, 4:25.
BY MR. THORNBURGH:
Q. Dr. Barbolt, the studies that you've listed for all of the designated topics that you believed were relevant to those topics you included within the list that we marked on the first day as 2241, correct?
MR. THOMAS: We marked the list --
MR. THORNBURGH: Oh, I'm sorry. I apologize. Maybe we ought to do that. The problem is I have handwriting on mine. I didn't bring another copy.
BY MR. THORNBURGH:
Q. Doctor --
MR. THORNBURGH: Let's go off the record for a sec.
(Whereupon, a discussion was held off the record.)
THE VIDEOGRAPHER: 4:26, off the video record.
(Short break.)

Page 548

THE VIDEOGRAPHER: Back on the video record. It's 4:42.
This begins Tape Number 5, Volume 2 of the videotaped deposition of Dr. Thomas A. Barbolt.
BY MR. THORNBURGH:
Q. Dr. Barbolt, we're going to mark as an exhibit a list of studies that you chose which you believe were relevant to the 30(b)(6) topics that you were designated to discuss. It's been marked as 2262.
(Document marked for identification as Exhibit T-2262.)
BY MR. THORNBURGH:
Q. Doctor, the 2262 list of studies are the studies that you chose that you believe were relevant to the topics you were designated to discuss, correct?
A. Yes, that's correct.
Q. Did anybody help you compile this list?
A. Yes.
Q. Who helped you compile the list?
A. Counsel's staff or Ethicon personnel. Ethicon personnel created the first list. This list

Page 549

was created after a review of that entire list of both literature searches of R&D central file. But, clearly, I didn't type all this and organize this and so on and so forth.
Q. Now, are you -- you didn't come prepared to talk about the number of the opinions that you expressed in your expert report, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That was not the intention.
BY MR. THORNBURGH:
Q. For instance, you didn't come prepared to talk about the biocompatibility or lack thereof of a mismatched mesh, right?
MR. THOMAS: Object to the form of the question. What is that?
MR. THORNBURGH: Language in his expert report.
MR. THOMAS: Sorry.
THE WITNESS: Mismatched mesh?
BY MR. THORNBURGH:
Q. Yes.
A. A lot of the topics in my expert report are along the same lines of the topics that

Page 550

we've been discussing here. There is a great deal of overlap.
Q. Well, in your expert report, on Page 12 of 27, you say: Movement of a mesh from its original site of implantation can result from compliance mismatching. This is a mesh that is stiffer in terms of bending rigidity than surrounding the tissue.
Are you prepared to talk about Ethicon internal documents; for instance, documents from Dr. Trzewik regarding the bio -- the biocompatibility or mismatching of mesh?
A. Yeah. I'd have to look at that -- I'd have to look at my expert report and then look at the reference to that particular article.
Q. Did you look at any of Dr. Trzewik's internal documents before you came here today?
MR. THOMAS: To prepare for this deposition today?
MR. THORNBURGH: Yes.
BY MR. THORNBURGH:
Q. I mean, if you want to go there, I'll go there. I'm ready to go there. If you want to talk about the tissue and the biomechanical properties of tissue compared to the biomechanical

Page 551

properties of mesh, which can cause increased inflammatory response as a result of mismatching, I am ready to do it. But I need to know from you if you're ready to do it.

A. Well, I came prepared to talk about the preclinical studies that we've got in front of us and behind us.

MR. THOMAS: Short answer is no.

MR. THORNBURGH: Okay.

BY MR. THORNBURGH:

Q. And that's one example of expert opinions that you have that you're not prepared to discuss today, correct?

A. That's correct.

MR. THORNBURGH: Are you going to give me a date where we can take Dr. Barbolt's expert deposition?

MR. THOMAS: To the extent that we intend to offer Dr. Barbolt in areas beyond the scope of the 30(b)(6) designation, yes.

MR. THORNBURGH: Well, I mean, I have all kinds of external Ethicon -- external scientific articles on porosity.

Now, porosity was an issue regarding preclinical studies, but he's offering opinions

Page 552

regarding pore size in his expert report. I want to have an opportunity to cross-examine him on non -- both internal and external documents that we have.

Now, if he's prepared to do that now, because we talked about porosity, then I'll do that. But if you're going to offer him up for an expert deposition on those issues, then I will reserve that for another time.

MR. THOMAS: I think that the option is to reserve for another time, and we'll decide whether another time is necessary. And if we don't agree, I think the magistrate has already spoken to that. But I feel confident we'll agree.

MR. THORNBURGH: So I don't need to go through like degradation studies and --

MR. THOMAS: No.

MR. THORNBURGH: -- studies that he wasn't prepared to talk about?

MR. THOMAS: Correct.

MR. THORNBURGH: We can raise that at another time and, hopefully, we can agree on a time before --

MR. THOMAS: A time and scope. I agree.

MR. THORNBURGH: A time before the

Page 553

trial, which is coming up.

MR. THOMAS: You owe me a jordi date, too.

MR. THORNBURGH: Well, I'm trying -- you just let me know yesterday, I think it was, that the date I proposed was not a good date, so I am trying to get another date for you. I hope to have that by today or tomorrow. Okay?

MR. THOMAS: Okay.

MR. THORNBURGH: I am going to give you a date before the trial.

MR. THOMAS: Okay. Are you finished now?

MR. THORNBURGH: No. I'm just trying to get some stuff on the record.

MR. THOMAS: What was the number of that last exhibit?

MR. THORNBURGH: 2262.

MR THOMAS: Thank you.

BY MR. THORNBURGH:

Q. Do you believe Ethicon should have done anything different in terms of the language they used in the IFU that we looked at regarding degradation and the inflammatory response?

MR. THOMAS: Object to the form;

Page 554

scope.

THE WITNESS: I am here to represent Ethicon with respect to these preclinical studies and their results.

BY MR. THORNBURGH:

Q. Based on the preclinical studies, including the five-year and seven-year data from the ten-year dog study and the other studies that showed chronic inflammation, do you believe that Ethicon should have done anything different, added any additional language, such that -- any additional language such that information would have been disclosed to physicians in the IFU?

MR. THOMAS: Object to the form of the question.

He's asking you from a preclinical perspective whether you would change the IFU.

THE WITNESS: Yes. As I indicated, the IFU is not the responsibility of preclinical.

It is responsibility of medical affairs folks, the regulatory folks, taking input from all areas of product development, including preclinical.

MR. THOMAS: He's asking you from a perspective of preclinical whether you would, from

Page 555

your preclinical experience, when you review the preclinical studies under the designations that have been made, whether you as Ethicon would change the IFU from a preclinical perspective.

THE WITNESS: No.

BY MR. THORNBURGH:

Q. Adding information in the IFU regarding the surface degradation is not a change that you think Ethicon should have made?

MR. THOMAS: Object to the form of the question.

THE WITNESS: It's not useful information for the surgeon when there is no impact on molecular weight and tensile strength of the fiber.

BY MR. THORNBURGH:

Q. Adding information to the IFU from a -- regarding the chronic inflammatory response that you observed in all of your preclinical studies, you don't believe that more definitive language regarding the chronic inflammatory response should have been added to the IFU?

MR. THOMAS: Object to the form of the question.

THE WITNESS: The tissue reaction to

Page 556

polypropylene-based material is well understood. It's discussed in detail, including the chronic inflammatory reaction to Prolene sutures in the 19 -- 1960s NDA submission.

The whole history of studies from the mid '60s to current day has demonstrated a very consistent tissue reaction profile to implanted polypropylene-based devices.

BY MR. THORNBURGH:

Q. So there is a chronic inflammatory response, not a temporary one, correct?

MR. THOMAS: Object to the form of the question.

THE WITNESS: It's well understood that the initial reaction is transient and can verge to a chronic inflammatory reaction and a fibrotic response with more or less inflammatory cell infiltrate, well documented in all the implantation studies.

BY MR. THORNBURGH:

Q. You don't believe that Ethicon should have added additional language in the IFU that discussed the chronic inflammatory response specifically using the word, chronic inflammatory response, in the IFU?

Page 557

A. No, I don't think that's necessary. I think all surgeons know that a permanent implant is going to be associated with some low level of chronic inflammatory reaction for the life of the patient.

MR. THORNBURGH: Move to strike after the word, no.

Pass the witness and reserve some time for cross-examination.

MR. THOMAS: Let's take a break, please.

THE VIDEOGRAPHER: It's 4:53. Off the video record.

(Short break.)

THE VIDEOGRAPHER: Back on the video record, 5:17.

- - -

EXAMINATION

- - -

BY MR. THOMAS:

Q. Dr. Barbolt, would you pick up Exhibit 2262, please.

A. Okay.

Q. And Exhibit 2262 is titled, "Deposition Subject Matter." And this is a document

Page 558

that you described towards the end of your deposition where you identified for counsel for plaintiffs all of those topics for which you gathered information to be responsive to the questions today. Correct?

A. Yes, that's correct.

Q. And this multi-page document obviously lists many studies. Do you have those studies with you here today?

A. Yes. They're in the various binders that you see around that are entitled with the specific subject matter topics as are listed in these sheets.

Q. How many boxes of binders did you bring to the deposition today?

A. Oh, I think there was 18 or 20.

Q. 18 or 20 binders?

A. Binders.

Q. The first one on the list is for the specifics of all testing related to the TVT products.

Now, you understand there are multiple TVT products?

A. Yes.

Q. And so you went back and searched for

Page 559

all the testing that you could find for all of the TVT products?
A. Yes. Each of the individual TVT products are -- and the data supporting their preclinical studies are assembled in individual binders and titled according to the TVT product.
Q. During the design and development stages, including but not limited to, at least for this section, it's porosity testing, particle loss, degradation, and leaching, correct?
A. Yes.
Q. And the first one that we have listed here is degradation. And you have notebooks here for degradation?
A. Yes.
Q. Correct?
And those notebooks contain 46 different documents?
A. That's correct. There are 40 different -- 46 different studies or documents related to potential degradation of TVT products.
Q. Now, the TVT, as you've explained in your examination, didn't come into existence until the late '90s, right?
A. That's right. The work started in

Page 560

the '97 time frame or so, and then I think the 510(k) approval was in early 1998.
Q. And the information that you list in response to the degradation designation begins in 1964; is that right?
A. Yes, that's correct.
Q. And it runs in chronological order all the way up until 2007, right?
A. Yes, that's correct.
Q. Why did you include studies that predated the TVT?
A. Well, the material used to manufacture TVT mesh is Prolene polypropylene filaments. And a great deal of work was done in the mid '60s and beyond, demonstrating biocompatibility of that product and essentially received FDA approval.
Q. What is an NDA?
A. An NDA is a new drug application. And at the time of the development of Prolene suture, polypropylene sutures were considered drugs.
Q. And did Ethicon go through a new drug application in order to have FDA approve the polypropylene suture that's now used in TVT mesh?
MR. THORNBURGH: Objection; beyond

Page 561

the scope.
THE WITNESS: Yes.
BY MR. THOMAS:
Q. And the first five studies in your degradation section are studies submitted to the FDA in connection with the Prolene suture NDA, correct?
A. That's correct.
Q. And let's talk about those briefly. Study of tissue reaction to the colorless and pigmented monofilament polypropylene suture in the rat, rabbit, and the dog.
Just tell me briefly what those studies are.
A. These were tissue reaction studies in three species of animals, with colored and non-colored suture, looking at tissue reaction over time.
Q. And how long were those studies?
A. The rat study was two years. That's the lifetime of a rat.
The dog study was two years. And the rabbit study was 90 days.
Q. And are those considered long-term studies?
A. The two-year rat as a lifetime study

Page 562

is certainly a long-term study, as with the dog study of a two-year duration.
Q. And what's the purpose of doing a tissue reaction study to a polypropylene suture in an NDA?
A. So for the purposes of a suture, the most important thing that needs to be determined is the tissue reaction of the material over time.
Q. And you have reviewed the tissue reaction studies from the NDA?
A. Yes.
Q. And are the tissue reaction findings for the polypropylene suture approved by the FDA similar to the findings that you have reviewed with respect to Prolene mesh?
MR. THORNBURGH: Objection to the use of the word, approved, as well as outside the scope of his designation.
THE WITNESS: The tissue reaction is very similar.
BY MR. THOMAS:
Q. Okay. And you understand that in order for Ethicon to be able to market this polypropylene suture, known as Prolene suture, the FDA had to approve the NDA?

Page 563

MR. THORNBURGH: Objection; move to strike.
THE WITNESS: Yes. That's an approval process. It's not like a 510(k) clearance.
BY MR. THOMAS:
Q. And as a matter of fact, in order to market this suture, this Prolene suture, Ethicon had to get approval from the FDA for the language that went in the IFU for the Prolene suture?
MR. THORNBURGH: Objection.
BY MR. THOMAS:
Q. Did you know that?
MR. THORNBURGH: Objection; lack of foundation, outside the scope.
THE WITNESS: That's correct.
BY MR. THOMAS:
Q. And the language -- strike that.
So after the NDA studies, you pick up a number of studies that begin in the '70s and go through the '80s, into the '90s, all the way up to the time when you start involving testing for the TVT device, correct?
A. Yes.
Q. And why did you include those studies in your degradation section?

Page 564

A. Those studies are part of the database that -- that shows that the tissue reaction to Prolene polypropylene filaments is very consistent over time.
Q. Now, in -- in the studies that have been conducted since 1964, when you conduct a tissue reaction study such as those listed in T-2262, is degradation something that's always a component of a study?
A. Yes, for absorbable or non-absorbable sutures. In this case Prolene suture is a non-absorbable suture. One needs to monitor what the appearance of the suture looks like over time so that one can conclude there's no visible evidence of degradation from these tissue reaction studies. That's always a component of a tissue reaction study.
Q. I am going to get into the seven-year dog study here in more detail in a little bit. But from any of the 46 studies that you identified in the degradation studies that you have brought here with you today, did you find any degradation of any Prolene suture or Prolene mesh that you saw created an increased inflammatory response?
MR. THORNBURGH: Objection.

Page 565

THE WITNESS: No. The tissue reaction is pretty consistent over time. And in many studies, there's a diminution of the tissue reaction over time. The kinds of qualitative characteristics seen with Prolene polypropylene suture are the very same kind of qualitative changes seen around filaments of the Prolene polypropylene mesh.
BY MR. THOMAS:
Q. And in any of the studies that you've identified in the 46 studies in the degradation section on T-2262, did you identify any failure issues with the mesh or the sutures due to any degradation of the mesh?
A. No. And I would point to Tab 5, where for the purposes of the Prolene suture NDA, there was a two-year study where Prolene suture was implanted and tensile testing was conducted, and there were no consistent changes in the strength of suture over time.
Q. So in these 46 studies that you were able to retrieve and review, did you find any issues with degradation of the polypropylene suture that makes up both Prolene suture and Prolene mesh to cause you any concern in the preclinical area about

Page 566

any adverse effects from the use of that suture due to degradation?
MR. THORNBURGH: Objection.
THE WITNESS: No.
BY MR. THOMAS:
Q. The next section in 2262 is called leaching. And, again, this is the specifics of all testing related to TVT products during the design and development stages, including but not limited to leaching.
And what is leaching, for the jury?
A. Leaching is the movement of a substance or substances from the body of an implant to the surrounding tissues.
Q. Now, the leaching section of your disclosure identifies 91 different documents in response to the leaching.
Why are there so many documents that you identified in response to the leaching issue?
A. Every implantation study is an opportunity to evaluate any potential consequence of leaching from an implanted device. And there are, as I recall, some studies in here that look at extracts of the device and administration of those extracts to animals to look at whether or not there

Page 567

is adverse reactions, for example, an intracutaneous reactivity test.

And these studies are conducted for products in variation -- in products over time and for many of the iterations of TVT mesh.

Q. Now, you have different categories of documents in the leaching section of this exhibit. You have one section called in vitro. What is that?

A. These are studies where the device is extracted to maximize leachables, and in this case you would say leachables/extractables, because sometimes the extraction mediums can accelerate the movement of substances from a mesh to the surrounding tissues.

These extracts are then tested in in vitro systems which are very sensitive.

Q. And what is an in vitro system?

A. In vitro system is a cell culture system. And with respect to these studies, they would be known as in vitro cytotoxicity assays.

Q. They're in a laboratory dish?

A. That's correct.

Q. Okay.

A. They are cells in culture and petri dishes, or nowadays in wells of 96 well plates where

Page 568

cells are incubated, and then the extracts are added to the cells.

And then an evaluation is made, as we discussed earlier, whether or not there's any impact on cell viability in accordance with standard USP scoring scheme, as we discussed earlier.

Q. If we look at your chart for leaching, beginning with Number 7 all the way through Number 34, you have in vitro studies that you've reviewed for the cytotoxicity of Prolene, correct?

A. Yes, that's correct.

Q. And you reviewed and prepared to testify about each of those studies, to talk about how they relate to the leaching issues, if any, associated with Prolene suture in mesh?

A. Yeah, that's correct. And we have talked about some of those today in the context of TVT mesh and the 510(k) submission of TVT original.

Q. Now, beginning with Number 35 all the way to Number 91, you have in vivo studies for leaching. What are the in vivo studies for leaching?

A. These -- these would be implantation studies where the materials are implanted in

Page 569

animals. And any leachables that would have adverse impact to the surrounding tissues would be revealed in a histomorphological evaluation of the section.

Q. Now, counsel made a number of questions about the fact that leaching is not a primary or called out endpoint in each of these studies.

Is leaching something that a pathologist looks for in any in vivo study?

A. Absolutely. A pathologist would be looking at the tissue reaction at the interface of the implant and the surrounding tissues. And if there were increased reaction, there would be a result of either the implanted material or any leachables or a combination of both.

Q. Now, the leachables we've talked about include the additive package that you were asked a number of questions about, correct?

A. Yes.

Q. The Santonox R, the DLTLP, and the others in the John Karl memorandum, do you remember those?

A. Yes, that's correct.

Q. And those additives have been in the product since the beginning, as that memorandum

Page 570

described. Do you remember that?

A. That's correct.

Q. And the in vivo section which begins on Number 35. Number 35 is an NDA study that's March 10, 1964, correct?

A. Yes.

Q. So from March 10, 1964 all the way up to March 11, 2010, you have in vivo studies where you've looked at the effect of any leachables on these in vivo studies?

A. That's correct.

Q. And the additives in the suture package that we talked about before at some length, all those additives were approved by FDA, weren't they?

MR. THORNBURGH: Objection.

THE WITNESS: FDA approved the original product, Prolene suture. And that suture contained those additives.

BY MR. THOMAS:

Q. And in any of the in vivo studies beginning on Page 35 -- on Number 35, all the way up to 91, did you find any adverse effects due to leaching from the Prolene suture or the Prolene mesh in those results?

Page 571

A. No.
Q. Now, why are the results from in vitro tests different from the results in in vivo tests sometimes?
A. In vitro tests are very quick to conduct. They are relatively inexpensive. However, they only provide directional information and not definitive information.
Q. What do you mean by that?
A. Well, they are studies conducted outside the body. Artificial environment.
Q. And if you have a positive cytotoxicity test in vitro, what does that mean to the question of whether the substance is going to be cytotoxic in vivo or in an animal?
A. Again, that would be a watch owl, that is a directional information. And then you would need to do more relevant in vivo studies to determine if the in vitro cytotoxicity translated it into any in vivo cytotoxicity or any adverse impact on wound healing.
Q. And in this case, as discussed in your direct examination, there was a positive cytotoxicity test in vitro for the TVT device, correct?

Page 572

A. That's correct.
MR. THORNBURGH: Objection. More than one.
BY MR. THOMAS:
Q. So what did Ethicon do when it had its positive cytotoxicity response to follow up on that?
A. Ethicon conducted a 28-day study in rats, looking at the implantation -- the tissue reaction to the -- or after the implantation of TVT mesh.
Q. You were designated as the person most knowledgeable regarding a 28-day intramuscular tissue reaction study in rats of polypropylene mesh in the TVT (Ulmsten) device (PSE 97-0197); is that correct?
A. Yes.
Q. And that's the study to which you just referred where Ethicon actually did an implantation study in rats to determine the extent to which the TVT mesh was cytotoxic in vivo, correct?
A. That's correct.
Q. And what was the finding of that study?

Page 573

A. The tissue reaction to the TVT mesh was very comparable to the non-in vitro cytotoxic Prolene flat mesh, in that there were -- was no impact on wound healing over time on the face of the implant.
Q. And what does that mean in terms of whether there is a cytotoxic effect of Prolene mesh in vivo?
A. Now, the least impact might be delayed wound healing, and that was not observed.
If there were a more severe impact as a result of leachables, that would have translated into an increased tissue reaction.
In other words, rather than minimal to mild reactions, we might have seen moderate to marked reactions.
Q. Was there any evidence in this 28-day rat study that you conducted to determine the extent to which the TVT mesh in the Ulmsten device was cytotoxic, that it was, in fact, cytotoxic in vivo? Any evidence at all?
A. No, there was not.
Q. Now, in the category that we have for that section, it's Category 4, and you don't need to go to it unless you want to.

Page 574

A. Okay.
Q. There are three other -- why don't you go ahead. It's about four from the back.
A. Four from the back. Okay. Yes. There's five tabs.
Q. And the first one is a study that we just discussed, the 28-day rat study?
A. Yes, that's correct.
Q. And that was a GLP study, correct?
A. Yes.
Q. What does it mean to be a GLP study?
A. A GLP study would be a study conducted in compliance with the FDA good laboratory practices regulations.
As we discussed earlier, all studies are conducted in accordance with SOPs and standard policies and procedures.
An FDA GLP study has an additional level of scrutiny, and that is outside, independent review of various phases of a study and a review of the final report in comparison to the raw data to ensure that they reflect individual animal data.
Q. The next three entries in Category 4, where you're the person most knowledgeable about this 28-day intramuscular study that we've just been

Page 575

discussing, deals with a mesh called Vypro mesh, and a cytotoxicity assessment for Vypro mesh.

What is Vypro mesh?

A. Vypro mesh is a composite mesh consisting of the filaments of polypropylene and polyglactin 910 yarn.

Q. And is Vypro mesh a hernia mesh?

A. Yes. It would be considered --

Q. And did a preclinical test on Vypro mesh determine whether it was cytotoxic?

A. Yes. As part of the development of Vypro mesh, some biocompatibility studies were conducted, and the in vitro cytotoxicity study was one of them.

Q. And what was the finding of the Vypro cytotoxicity test?

A. Vypro mesh was cytotoxic in vitro.

Q. And so what did the company do? Did it not market it?

A. Well, as part of the biocompatibility assessment, they then conducted a intracutaneous reactive study looking at extracts of the suture that would get leachables and extractables and then ejected them into the skin of rabbits to look at evidence of local irritancy.

Page 576

Q. And what was the finding from that intracutaneous study?

A. It was negative. There was no evidence of irritancy. The reaction was negligible.

Q. So once it passed the intracutaneous in vivo test, did the company then get clearance to market the product?

A. Yes.

Q. So at least in one other circumstance in which you have been involved and the company has been involved, there has been a positive cytotoxicity test for a mesh that you followed up. And then after doing in vivo testing, you determined that it's appropriate to market the mesh?

A. Yes. And I should say in addition to the intracutaneous reactivity test where extracts are injected into rabbit skin, of course there was an implantation study that we discussed at length, I think these last few days, and that is the 91-day study where the tissue reaction to Vypro mesh was compared to many other meshes, and the tissue reaction was found to be acceptable with appropriate tissue integration.

Q. The tissue reaction study you're talking about now is T-2242, titled "Exploratory

Page 577

91-Day Tissue Reaction Study"; is that right?

A. Yes. It's tab -- its Tab 5 here on this list.

Q. And that tests the Prolene 5 mil mesh, correct?

A. That's correct.

Q. And the Vypro mesh, a couple of versions of the Vypro mesh?

A. Yes.

Q. And there were no cytotoxic findings as a result of that 91-day study for either Prolene 5 mil mesh or the Vypro mesh, correct?

A. That's correct. There was no evidence of increased tissue reaction in the Vypro study in spite of there being evidence of in vitro cytotoxicity in a manner very similar to a TVT mesh.

Q. The last document on the leaching schedule, going back to where you were, Number 6, is a May 8, 2013 document, and it's titled "Biocompatibility Risk Assessment For The Gynecare TVT Product Family."

What is that?

A. Let me catch up to you, David. What's the tab number?

Q. Tab 6.

Page 578

A. Tab 6. This was a technical file that was updated just recently at the request of the European Union for the whole family of TVT products, essentially a compilation of the history of TVT family of products, outlining component materials, tests -- biocompatibility testing that was appropriate in accordance with tissue contact categories, and an evaluation of the biocompatibility results coming to a final assessment of whether or not the biocompatibility of Gynecare family of products conducted, in light of the current version of ISO 10993 standards, not realizing that these standards changed every five years and that the standards in place in 1997 would be different than the ones in place in 2013.

So some of the goal of this exercise was to apply current 2013 standards against the biocompatibility testing program conducted for TVT family of products to see if, in fact, the biocompatibility risk assessments done at the time still hold.

Q. And that would relate also back to the testing done on polypropylene sutures back in 1964 with the NDA, wouldn't it?

MR. THORNBURGH: Objection.

Page 579

THE WITNESS: Yes, that's correct. In the same manner that we've discussed and leveraged that early data on poly -- Prolene polypropylene fiber for suture, it's also relevant for Prolene meshes and TVT.
BY MR. THOMAS:
Q. And does the biocompatibility risk assessment for the Gynecare TVT product family of May of 2013 include a leaching component?
A. Yes.
Q. And so this product -- the studies and the documents that you have in the leaching section of your documents that you brought with you today covers some 49 years, correct?
MR. THORNBURGH: Objection.
THE WITNESS: Yes.
BY MR. THOMAS:
Q. And in those 49 years of 91 documents, did you find anything that suggests that there's anything leaching from polypropylene sutures -- excuse me. Strike that.
In your 49 years of documents, you covered some 91 different documents. Did you find any evidence of any leaching in vivo that led to any adverse reaction in a preclinical study?

Page 580

MR. THORNBURGH: Objection.
THE WITNESS: No.
BY MR. THOMAS:
Q. The next section that I have in this disclosure, which is T-2262, is the specifics of all testing related to TVT products during the design and development stages, including particle loss.
Now, tell me the difference between the clinical and the preclinical analysis of particle loss.
MR. THORNBURGH: Objection.
THE WITNESS: The preclinical assessment of particle loss is one that can be done in any implantation study where the implant is visualized against the surrounding tissue. And if there are any particulates there, they would be observable.
I am not sure about the clinical arena. I don't know that I can speak to that.
BY MR. THOMAS:
Q. Okay. The clinical arena involves humans, and that's not work that you do?
A. That's correct.
Q. And you are aware of the particle loss issues insofar as they relate to preclinical

Page 581

testing?
A. Yes.
Q. And why did you pick the documents that you have here, beginning in 1964, the 38 documents, going all the way up to 2007? Why did you include those?
A. Particles were observed in the Prolene suture NDA submission. And as I pointed out this morning, they resulted in an inflammatory reaction very similar to that reaction around the filaments of the suture.
Q. You talk about fragments and you've talked about particles. Are fragments and particles different?
A. As I mentioned this morning, I see a big difference there.
A fragment of a suture is likely to have been related to the swaging process or the cutting lengths of suture, or a fragment of suture gets attached to the suture and then gets implanted with it.
That's different than the microparticulates that we discussed earlier, looking at data from the seven-year dog study.
Q. And so the 38 studies that you've

Page 582

included in your section of particle loss from the period, 1964 to 2007, you've looked for the extent to which there's been any adverse consequences noted in preclinical studies from any kind of particle loss of sutures and mesh?
A. Yes, although fragments are noted in the NDA submission and in the Postlethwait study that we discussed earlier. In the early going, in the development of Prolene suture, I've not seen personally in any of the implantation studies that I've conducted any sort of fragment of filament next to a filament in an implantation study.
Q. And you talked before about the particle in the NDA study and the kind of reaction that -- tissue reaction with respect to that particle.
With the particle in the NDA study, did you find any adverse inflammation or tissue reaction that had any consequences to you for a preclinical perspective?
A. No.
Q. Why?
A. It was the same kind of reaction around the fragment as there was around the suture.
Think about a tissue reaction around

Page 583

the earth and a tissue reaction around the earth and moon. The tissue reaction around the earth is around the interface of the earth and the atmosphere. And then there is the moon on the side of the earth with a very similar reaction around its interface with substance and atmosphere.

Q. You answered the question at least seven or eight times today about whether more material implanted leads to an increased tissue reaction, and you said as a general proposition, that's true. Is that fair?

A. Yes, I think so. I think that's a general principle. Again, as I also mentioned, the details and particulars need to be determined on the basis of an implantation study.

Q. And -- and how much additional material -- strike that.

Are you able to evaluate the extent to which additional material creates a tissue response that's unacceptable from a preclinical study?

A. Yes. I think in every implantation study, one can make that determination.

Q. In your evaluation of all of the studies in the particle loss section of your

Page 584

designation, the 38 studies over 43 years, did you find any unacceptable tissue response to any particles in those studies?

A. Yeah. The only --

MR. THORNBURGH: Objection.

THE WITNESS: The only studies that even talk about particles or fragments is the NDA work in a study done in 2002, Tab 33, that was done specifically to look at whether or not particles would be present after implantation of lengths of TVT tape. And, in fact, none were observed.

BY MR. THOMAS:

Q. Would you get 2260 in front of you, please. That's the Pariente study. I don't have the number of the rabbit study.

MR. THOMAS: Do you happen to have that, Dan?

MR. THORNBURGH: The test number or the exhibit number?

MR. THOMAS: The exhibit number. I do have it. I'm sorry.

MR. THORNBURGH: 2133.

BY MR. THOMAS:

Q. 2133. Can you get 2133 and 2260? 2133 is the March 5, 2003 rabbit test, and 2260 is

Page 585

the Pariente study.

A. I've got the 2260. I'm looking for 2130.

Q. I'll get this copy to you.

A. Maybe it was discussed yesterday, and it's in this stack, yeah. I can probably get it, David.

Q. It's all right. I've got another copy.

The Pariente study is the particle loss study that counsel discussed with you at length at T-2260.

If you go to the first page of T-2260, down in the lower right-hand corner, it reads: Mechanical testing was performed with a 7-centimeter length sample (n=5) on an Instron 4466 with a 500-Newtons sensor using the software Series IX-7 to program the setup.

What is an Instron machine?

A. An Instron machine is a piece of equipment that can determine the tensile strength of a fiber by pulling at both ends and determining the strength at -- the force at which it breaks.

Q. And how did Pariente use an Instron machine to test the extent to which particles were

Page 586

shed from the meshes that they tested?

A. Well, it looks like he put each mesh on the Instron machine and pulled it until it broke.

And as I look on Table 1 of that study, it looks like each of the meshes were pulled, as one might expect, a different peak load, depending on their biomechanical characteristics.

Q. And at what point in this process were particle loss measured? Are you able to tell that?

A. Could you repeat the question?

Q. Yes. At what point in this experiment were the particle losses measured?

A. I think at break.

Q. Okay.

A. I think at break. As I look at this Figure 3, there's a break, obviously, and then there's a drop in force because there is a break.

Q. Is 2260 a preclinical study that Ethicon conducts to evaluate particle loss?

A. Ethicon did not conduct this study.

Q. Does Ethicon -- strike that.

Is this a preclinical study?

A. This is kind of bench-top biomechanical testing.

Page 587

Q. What is the difference between bench-top biomechanical testing and preclinical testing?
A. Well, I guess it can be considered preclinical because it's done before, you know, the product gets to clinic. But it's different than preclinical in my mind that has to do with in vitro or in vivo experimental studies with products in animals.
Q. Okay. And why is it important to you to measure products in vitro or in vivo in animals?
A. Well, because any bench-top is an artificial environment designed to look at a specific parameter under certain conditions. And in my mind, an in vivo study where there is an implantation of a product, it's more clinically relevant because it simulates the patient environment.
Q. If you look at T-2130, this is the two-week rabbit study; is that correct?
A. 2133?
Q. Yes.
A. Yes, a two-week rabbit study.
Q. And if you look at the abstract on Page 3, the objectives of the study were to compare

Page 588

the mechanical strength and histological response of Prolene mesh and Prolene Soft mesh in skeletal muscle of the rabbit, correct?
A. Yes.
Q. And this is the same Prolene mesh that's used in TVT?
A. Yes, that's correct.
Q. And one of the specific endpoints of this study, this two-week rabbit study, T-2130, is to evaluate the extent to which the mesh shed particles inside the rabbit, correct?
A. Yes, that's correct.
Q. And how did the study do that?
A. The implant site was explanted and the tissue reaction was assessed. And, obviously, that would include the implant and any particulates that might be present, as that was one of the called out objectives in this particular experiment, although for me, any implantation study I would be looking for particulates, but this was called out in this study.
And so they would look at the tissue reaction to the mesh itself and any evidence of particulates in the surrounding tissue.
Q. If you go to Page 35 of that study,

Page 589

T-2130?
A. That's 33. 2133?
Q. Yes.
A. You keep saying 30.
Q. I'm sorry. Thank you.
A. What was the page number?
Q. Page 35.
A. Okay.
Q. You see under the category, approximate average thickness of fibrous tissue located between the mesh fiber bundles -- strike that. Let me start over again.
On Page 35 of Exhibit T-2133, there is a table called "Histological Observations," correct?
A. Yes.
Q. And what are histological observations?
A. These are observations by the study pathologist looking at evidence of tissue reaction and integration and the evidence of fibrosis or any other impact of the surrounding tissues.
Q. And there is a category that's there. It says: Inflammatory cell infiltrates only associated with the mesh.

Page 590

What is that? Right in the middle.
A. Yeah. It looks like they're calling out the tissue reaction associated with the mesh versus a tissue reaction to the skeletal muscle which was injured during the implantation process.
Q. And in the far right-hand corner -- excuse me -- the far right-hand column, there is a specific category for mesh particles within muscle.
And for each one of these animals, they specifically look in the histology to try to identify any particles that may have been in the rabbit in two weeks; is that correct?
A. That's correct.
Q. And do they find any particles in the histology for any of the rabbits?
A. No. No particles were observed for any -- for any -- at any implantation site.
Q. And this is a two-week study. Does the fact that this is a two-week study as opposed to a six-month study or a ten-year study have any impact on whether this is a valid study to determine the extent to which mesh particles may be found after implantation of mesh?
A. I think at a two-week post implantation period is sufficient time for a tissue

Page 591

reaction and a fibrotic response to occur around any particulate if it were present.
Q. Okay. And the histology in this two-week rabbit study, 2133, was consistent with all of the other Prolene tissue response tests that you've gotten since 1964, correct?
A. Yeah, that's correct. If you look at the inflammatory cell --
MR. THORNBURGH: Objection. Sorry. If you can just give me a hair of a second --
THE WITNESS: I'm sorry.
MR. THORNBURGH: -- I'd appreciate it. I've got to get an objection in.
THE WITNESS: That's fine.
BY MR. THOMAS:
Q. Let me read the question again.
And the histology in this two-week rabbit study, 2133, was consistent with all of the other Prolene tissue response tests that you've gotten since 1964, correct?
MR. THORNBURGH: Objection.
THE WITNESS: Yes. So if you look in the column, inflammatory cell infiltrates only associated with the mesh, for every mesh, that would

Page 592

be Prolene Soft mesh, Prolene mechanical cut, which is TVT mesh, and Prolene ultrasonic cut mesh, which would be a laboratory-made device to simulate a different cutting process for TVT tape, all of the inflammatory reactions were minimal.
And, further, if you look at the approximate average thickness of fibrous tissue, what I would call fibrosis in studies that I've read, located between the mesh fiber bundles -- and this is measured -- attempted to be measured in microns, as we've seen in some early report -- pathology assessment schemes -- the results at 7 and 14 days are -- there's no distinct encapsulation for any product.
BY MR. THOMAS:
Q. What does that mean, no distinct encapsulation?
A. That the fibrotic response was relatively minimal.
Q. Let's talk about encapsulation quickly. I am jumping around a little bit, and I apologize.
In questions yesterday from counsel in -- with respect to T-2242, the exploratory 91-day tissue reaction study, there were some macroscopic

Page 593

observations of encapsulation that were observed that were not confirmed upon histological review. Is that fair?
A. That's correct. I recall that discussion.
Q. And you were the person who conducted the histological review, correct?
A. Yes.
Q. And how is it that what might appear on a microscopic level to be encapsulation, upon histologic review, may prove something else altogether?
A. Yeah. The deficiency of a macroscopic observation is that it cannot see through the tissue. For example, if I were to put this piece of paper on top of this -- the title of this document, you would not see that.
That would be the result of a macroscopic observation. You could only see the surface. And that's a directional information, as I mentioned.
The histomorphological evaluation of the implant site looks at a cross-section of the implant, top to bottom, through and through. So not only can the pathologist see the surface coating,

Page 594

but they can see all the other components through the mesh implant.
Q. Okay. So which is the more valid observation?
MR. THORNBURGH: Objection.
THE WITNESS: The histo -- the histomorphological evaluation is the definitive result.
BY MR. THOMAS:
Q. Okay. Sorry to jump around.
Going back to the Pariente study, which was T-2260, and the Ethicon two-week rabbit study, which is T-2133, which is the better study from a preclinical perspective for Ethicon to evaluate the safety and efficacy of its product?
A. I always lean towards in vivo studies to simulate a patient population.
Q. And what value to you in preclinical context is 2260, the Pariente study?
A. It's informational.
Q. Any value to you from a preclinical perspective other than what they state?
A. No.
Q. The next section in your disclosure is the porosity section. And the porosity section

Page 595

for the development of mesh products only contains 12 entries. And counsel inquired at length about why you only had 12 studies to support the porosity testing for the TVT device.

And I think we've established pretty clearly that T-2247, the 1973 rabbit study, is the first study conducted by Ethicon on Prolene mesh for tissue reaction, correct?

A. Yes, that's correct.

Q. And we went through that study at some length.

Is the tissue reaction profile found in 2247 for Prolene mesh used in TVT consistent with the tissue reaction profile found in other Prolene mesh marketed by Ethicon?

MR. THORNBURGH: Objection.

THE WITNESS: First, is that exhibit that you called out the '73 study?

BY MR. THOMAS:

Q. Correct.

A. Then the response would be that the tissue reaction profile reported in the 1973 study represents the kind of tissue reaction seen in studies conducted since then.

Q. Including the 91-day rat study using

Page 596

the 5 mil mesh?

A. That's correct.

Q. And in all of the porosity studies that are listed, the 12 that are listed here, the finding of tissue reaction with respect to Prolene mesh, does it meet the same profile?

A. Yes.

Q. And what is that profile?

A. A relatively mild reaction, an acute phase, which is transient and passes, because the implant is biocompatible. The tissue reaction transitions to a low level chronic inflammatory reaction and a fibrotic reaction that encapsulates elements in a three-dimensional way of the mesh.

And that tissue reaction is sustained through the -- for the duration of each of the studies, and in many of those studies, there is a diminution of that reaction over time.

Q. And that diminution in the reactions or the change in the reactions that you've just described is what you've described to counsel as a long-term chronic reaction?

A. That's correct.

Q. And does the long-term chronic reaction present any risk from a preclinical

Page 597

perspective?

A. No.

MR. THORNBURGH: Objection.

BY MR. THOMAS:

Q. Now, you were questioned at some length about why you haven't done any more porosity studies on 6-mil Prolene mesh since the 1973 study. Why is that?

A. Well, there's -- in preclinical science, there are limitations on the number of animal studies that can be conducted. USDA animal welfare regulations require experimental institutions to justify the use of additional animals. And part of that justification is making a statement that this work has not been conducted previously, and if so, then further studies are not allowed.

Q. In the 91-day rat study, T-2242, there is an extensive section and literature research -- literature search contained in the data for that study. Do you recall that?

A. Yes.

Q. And why is that literature search set forth in that study?

A. Part of the --

Page 598

MR. THORNBURGH: Objection.

THE WITNESS: Each research institution has an institutional animal care and use committee whose job is to have oversight over all experimental studies and as part of that oversight, requires a literature search of either the public -- well, the public and internal databases to make sure that previous studies that have been conducted will not be repeated.

BY MR. THOMAS:

Q. After Ethicon obtained the results from the test in 2247, which is a 1973 rabbit test, was there any reason to conduct further tissue reaction studies for this Prolene flat mesh?

A. No. And all tissue reactions conducted on various iterations of Prolene mesh over time showed a very comparable tissue reaction as described in the 1973 study.

Q. And so the 12 studies that you site in connection with your porosity analysis all have a consistent tissue reaction profile?

A. Yes.

Q. And is the tissue reaction profile that is described in those 12 studies consistent with the language in the IFU that you talked about

Page 599

at length with counsel for the plaintiff?
MR. THORNBURGH: Objection.
THE WITNESS: Yes, I think so.
BY MR. THOMAS:
Q. The next category that you were asked about -- excuse me -- that you were designated on is Section BB. And you were asked to provide the specifics of all clinical, preclinical, and medical testing related to all of the TVT products, and you were responding to the preclinical piece of that.
Do you recall that?
A. Yes, I do.
Q. So as a part of that, you gathered all of the testing that Ethicon did for each of the devices. Is that fair?
A. That's correct.
Q. And to the extent that Ethicon leveraged prior testing from Prolene sutures, you've also identified that?
A. That's correct. They're all relevant.
Q. Okay. And you did that for the TVT device, correct?
A. Yes.
Q. You did that for the TVT-O device?

Page 600

A. That's correct.
Q. You did that for the TVT-Secur device?
A. Yes.
Q. You did that for the TVT-E device?
A. That's correct.
Q. And the TVT-A device?
A. That's correct.
Q. And this included any new component parts that were added to any of the TVT devices. You were asked by the plaintiffs to provide that information for all of the tools that might accompany those devices?
A. That's correct.
Q. And you have notebooks of all the tests that were conducted on each of those TVT devices here today to talk about the -- every aspect of the -- any new components to any of the TVT devices?
MR. THORNBURGH: Objection.
THE WITNESS: Yes.
BY MR. THOMAS:
Q. And, also, as a part of this, you have biocompatibility risk assessments for each of these devices. Isn't there?

Page 601

A. Yes.
Q. And you're prepared to talk about all the biocompatibility testing done for each of those devices?
A. Yes.
Q. Now, next category is Category CC, and you were asked to be the person most knowledgeable, Rule 30(b)(6) designee, for animal testing records for biocompatibility as part of the design of the product. Correct?
A. Yes.
Q. And here you have listed 64 different documents, correct?
A. Yes.
Q. And you're prepared today to talk about all of these 64 documents concerning the animal testing records for biocompatibility as a part of the TVT products?
A. Yes.
MR. THORNBURGH: Dave, what section are you on?
MR. THOMAS: CC, which is called animal testing records for biocompatibility as part of the design of this product.
BY MR. THOMAS:

Page 602

Q. Now, Category DD asks for the person most knowledgeable concerning the evaluation of data and results of any preclinical studies and testing regarding your TVT products and states that all documents responsive to this category have already been identified.
And so all of the documents that we have just been through are responsive to this category, and you have those here with you today?
A. That's correct.
Q. Category EE says the development and coordination of any preclinical studies. And to the extent that you have studies responsive to this category, those have been identified in previous categories as well, and they're here with you today?
A. That's correct.
Q. The next category is one that we spent a good deal of time on. Next category deals with the identity of, the location of, and the substance of any and all studies, data, and/or other evidence that form the basis of the following claim/statement included in the attached instructions for use for the TVT products.
And the statement is that animal studies show that implementation of Prolene mesh

Page 603

elicits a minimal inflammatory reaction in tissues, which is transient and is followed by the deposition of a thin, fibrous layer or tissue which can grow through the interstices of the mesh, thus incorporating the mesh to adjacent tissue.

Your first tab is 1964. Why do you include information from 1964 in the materials that you designate in response to this category?

A. As -- as we discussed earlier --

MR. THORNBURGH: Objection.

THE WITNESS: -- the Prolene polypropylene suture forms the basis for the Prolene polypropylene mesh, the same Prolene polypropylene filament.

And so any studies that are relevant to the tissue reaction of suture are relevant in a way to the filaments that comprise Prolene polypropylene mesh.

BY MR. THOMAS:

Q. And the tissue reaction studies that were part of the NDA were reviewed by FDA in the NDA approval process, correct?

A. That's correct.

Q. And FDA ultimately approved the use of the Prolene suture for sale in the United States

Page 604

under the new drug application?

A. That's correct.

MR. THORNBURGH: Objection.

BY MR. THOMAS:

Q. And FDA ultimately approved the language that appears up above in the IFU in substance for the Prolene suture?

MR. THORNBURGH: Objection.

THE WITNESS: That's correct.

BY MR. THOMAS:

Q. And the 44 documents that you cite below this category, are all of these consistent with the language that appears in the IFU on which you're designated?

A. Yes.

Q. Now, the next category says the material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes.

Now, this language was also part of the original instruction for use for the polypropylene -- excuse me -- the Prolene suture?

A. That's correct.

Q. And this language was specifically approved by the FDA in its approval of the Prolene

Page 605

suture NDA, correct?

MR. THORNBURGH: Objection.

THE WITNESS: Yes, that's correct.

BY MR. THOMAS:

Q. And that was based upon the studies, one through five, that appear under this section of the disclosure?

A. Yes, that's correct. Long-term implantation studies and long-term retention of breaking strength.

Q. Now, if you go to Tab 6, the Miller study, what did you learn about the -- the issue of tissue enzymes in the advent of polypropylene sutures?

A. This is a paper in the open literature. We can look at it in detail if we need to, which, as you say, is Tab 6.

But I recall there's some language in there that talks about the Prolene polypropylene suture is resistant to the effects of tissue enzymes.

Q. And what was it about other sutures in use at the time that created a risk of degradation from tissue enzymes?

A. Yeah, this is very significant,

Page 606

because at the time, another monofilament suture, as Prolene suture, was catgut suture, and that was made of intestinal collagen from animals, and it's known to degrade over time.

So to have a suture that doesn't degrade in the presence of tissue enzymes, whether it's placed in the stomach or part of an inflammatory process or it's in the pancreas, that's something that would be new to many surgeons.

Q. Now, you talked at length about the fact that molecular weight and tensile strength are the two key components for you in preclinical to evaluate the extent to which degradation is a significant event, correct?

A. Absolutely.

Q. In any of the 59 -- excuse me -- 49 papers, from 1964 to 2013, did you identify any Prolene suture or mesh that underwent degradation in the form of change in molecular weight or loss of tensile strength that caused you concern from a preclinical perspective?

MR. THORNBURGH: I just want to object to the representation that even molecular weight studies were even done in the 40 or so -- 40 -- however many studies that are in this list.

Page 607

Are you representing to the Court that molecular weight studies were done in each one of these tests?
MR. THOMAS: No, I'm not. I am asking --
MR. THORNBURGH: Objection. Move to strike.
That's a representation that you've been making to this jury this entire time.
MR. THOMAS: Please. No speeches to the jury. That's not appropriate. You know that.
MR. THORNBURGH: It's fair representation, honest ones.
BY MR. THOMAS:
Q. Dr. Barbolt, with respect to the 49 documents that you've identified in response to this issue of the materials not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes, did you find any information in any form that caused you concern that there was degradation from a preclinical perspective that caused you concern?
MR. THORNBURGH: Objection.
THE WITNESS: No.
BY MR. THOMAS:

Page 608

Q. Category 4 is the person most knowledgeable regarding a 28-day intramuscular reaction study.
We already talked about that. That's the study that you did after the positive cytotoxicity study in the Ulmsten device where you then did the intramuscular study to determine the extent to which the TVT was going to be cytotoxic in vivo.
A. That's correct.
Q. And that result was negative?
A. That's correct. There was no evidence of in vivo cytotoxicity.
Q. And you were the person who ran that test?
A. Yes. I was the study director and study pathologist.
Q. And you're prepared to talk about that test today?
A. Yes.
Q. In questioning yesterday, you were shown a variety of grading scales used by pathologists over the years to evaluate tissue response from various implantation studies. Do you recall that?

Page 609

A. Yes.
Q. As a pathologist reviewing the data that's been provided to you, are you able to review that data and determine the extent to which those various grading scales can be analyzed to reach a common result?
A. Yes.
Q. And tell me how you do that.
A. Well, you look --
MR. THORNBURGH: Objection. I don't even understand the question.
BY MR. THOMAS:
Q. You can answer the question.
A. Answer the question?
You look at the individual observations from each of the studies and you make a judgment based on the description and the severity scores that might be associated with that observation about what really happened.
So for me to go back and look at a study conducted under the Sewell scheme that we talked about yesterday, I could reinterpret those results in a manner that I would have recorded the result if I were going to be doing that work today.
It takes some work, and it needs to

Page 610

be done by a person trained in histomorphological evaluation, but it's not a difficult task.
Q. Why do pathologists record in detail what they observe?
A. That forms the basis for their interpretation of the study results.
Q. And does that allow someone to come behind them to analyze the extent to which they agree with those findings?
A. Absolutely. And the -- and the -- and the safety mechanism for that is the fact that the slides are considered the ultimate raw data in a pathology study.
This allows another pathologist to go behind the study pathologist and re-read those slides to generate their own set of data and their own conclusions to see how they compare with the original study pathologist. It's done very commonly.
Q. And is that the reason why you try to preserve slides where you can of these kinds of studies?
A. Yes. Yes. Every intention is to maintain raw data as long as possible.
Q. Now, you talked before in the 91-day

Page 611

study, T-2242, you were the pathologist who reviewed those slides, correct?
A. That's correct.
Q. And you talked about how you may have either recorded the data on an Excel spreadsheet or perhaps made notes before you made your final report; is that right?
A. That's correct.
Q. And I think you also said that you didn't retain any of the notes that you might have kept on your initial findings that were later recorded in the document which is 2242. Is that fair?
A. That's correct.
Q. Is that common?
A. That's standard industry practice.
Q. Tell me what you mean by "standard industry practice."
A. Well, pathologists have an opportunity to go back to the original data, that's the slide, this week, next week, some other period -- point in time.
Many times studies occur over a long period of time, and a pathologist may be involved in a lot of different studies. So at the end of a long

Page 612

period of time, a study pathologist may want to go back and revisit the original observations from the first look.
And maybe something that's -- that is observed at a later time point now causes the pathologist to reevaluate those earlier slides. There could be many iterations of slide evaluation.
But when I say it's standard industry practice, it's the signed individual animal observations that becomes the raw data for the study report.
Q. Okay. Why are your notes not raw data?
A. Because they can change over time.
Q. Okay. And what is raw data to a pathologist insofar as the histology report goes?
A. The slides.
Q. And what significance is the report that the pathologist -- the pathologist makes in the study?
A. I don't understand the question.
Q. Okay. What does the histology report represent insofar as your review of the slides?
A. It represents the raw data signed off by the study pathologist. And that's the results

Page 613

which the study pathologist believes reflects the microslides.
Q. In your training, education, and experience in your area of expertise, do histologists keep the notes that they initially make when they ultimately record their findings in their final report?
A. No.
MR. THORNBURGH: Objection.
Are you talking about histologists that have a litigation hold in place?
THE WITNESS: It wouldn't matter to me.
MR. THOMAS: In 2000, the year, 2000.
MR. THORNBURGH: It wouldn't matter to you?
MR. THOMAS: Let's take a break.
THE VIDEOGRAPHER: Going off the video record at 6:23.
This concludes Tape Number 5, Volume 2 in the videotape deposition of Dr. Thomas A. Barbolt.
(Short break.)
THE VIDEOGRAPHER: We're back on the video record. It's 6:34.

Page 614

This begins Tape Number 6, Volume 2 of the videotape deposition of Dr. Thomas A. Barbolt.
BY MR. THOMAS:
Q. Dr. Barbolt, in response to an objection from Mr. Thornburgh, you volunteered it wouldn't matter to you if there was a litigation hold in place about whether you keep notes.
Have you ever destroyed any documents or discarded any documents that you knew were subject to a litigation hold in this case?
MR. THORNBURGH: Objection; asked and answered.
THE WITNESS: No.
BY MR. THOMAS:
Q. You were asked a number of questions about preclinical tests and symptoms of delayed wound healing, ulceration, and increased inflammation.
Of the studies that we have just been through in great detail, did you see any evidence of delayed wound healing in the tissue integration studies that you reviewed that you would attribute to Prolene mesh?
MR. THORNBURGH: Objection.

Page 615

THE WITNESS: No.
BY MR. THOMAS:
Q. Well, same question for Prolene sutures.
A. No.
Q. In all of the studies that we've just described in some detail, were you able to find any evidence of ulceration in those animal studies that you would attribute to Prolene mesh?
A. No.
Q. Were you able to find any evidence of ulceration due to Prolene suture in those studies we just described?
A. No.
Q. And, finally, of all of the studies that we just went through in great length, did you find any increased inflammatory response that you were able to attribute to any leachables from Prolene suture?
MR. THORNBURGH: Objection.
THE WITNESS: No.
BY MR. THOMAS:
Q. Were you able to find any increased inflammatory response that you were able to attribute to leachables from Prolene mesh?

Page 616

A. No.
Q. Were you able to find any increased inflammation that you were able to attribute to particle loss for Prolene suture?
A. No.
Q. Were you able to find any increased inflammation that you were able to attribute to particle loss from Prolene mesh?
A. No.
MR. THORNBURGH: Objection.
BY MR. THOMAS:
Q. Were you able to find in all of those studies that we've just discussed any instance of delayed wound healing that you were able to attribute to degradation of Prolene suture?
A. No.
Q. How about any degradation of Prolene mesh?
A. No.
Q. With respect to ulceration, were you able to find evidence in any of the studies that we've just identified any ulceration that you were able to attribute the degradation of Prolene mesh?
A. No.
Q. And, likewise, with respect to

Page 617

degradation, were you able to identify in any of the numerous studies that we've just identified any increased inflammation that you were able to attribute to Prolene mesh?
A. No.
(Document marked for identification as Exhibit T-2263.)
BY MR. THOMAS:
Q. Let me show you what I've marked as Deposition Exhibit 2263.
2263 is the binder that you prepared for the seven-year dog study. Do you see that?
A. Yes.
Q. And the seven-year dog study is what counsel asked you many questions about I guess earlier today. Is that fair?
A. Yes.
Q. And I want to go through that study with you a little bit.
I'll represent to you that this document has in it a number of documents that hadn't been marked, and that's why I marked it all together. And just because it's going to be easier -- and I'll try to save time -- I'm going to mark the final report separately, because I can't

Page 618

put my hands on it very quickly, and I don't want to keep you here any longer than I have to.
(Document marked for identification as Exhibit T-2264.)
MR. THOMAS: I'll mark 2264 the same report that we marked earlier today. This didn't have the folded back front page.
Counsel, it's 2264.
BY MR. THOMAS:
Q. Exhibit 2264 is the October 15, 1992 report that says: Seven-year data for ten-year Prolene. Do you recall that?
A. Yes.
Q. And you were asked a number of questions earlier about this document concerning the scanning electron microscopy conducted at that time. Do you recall that?
A. Yes.
Q. And you identified in the report where someone observed cracks on the surface of some Prolene mesh. Fair?
A. Yes.
Q. Dr. Barbolt, when does a surface crack in Prolene mesh raise preclinical issues that need to be investigated further?

Page 619

A. When there's a loss in tensile strength. I think that's the -- that would be the -- the final straw. There might be impact on molecular weight, but if there was no impact on tensile strength, that would be the -- that would be the -- the definitive endpoint.
Q. Why are surface cracks alone, without any evidence of tensile strength issues or molecular weight, why don't they raise preclinical issues for you?
MR. THORNBURGH: Objection.
THE WITNESS: Because they don't have an impact on molecular weight, which would be evidence of degradation of polymer chains. And if there were degradation of polymer chains, that would be reflected in a loss in tensile strength.
So those two endpoints are key preclinical endpoints. Other endpoints are informational. They're not so important if they don't have an impact on those two endpoints.
BY MR. THOMAS:
Q. And tell the jury what molecular weight is.
A. Molecular weight is a measure of the length of the polymer chain. The longer the polymer

Page 620

chain, the heavier its weight. And biomaterials are comprised of many chains of polymers. So a higher molecular weight would suggest a polymer, in this case, fiber, with a pretty high tensile strength.
Q. And what does a change in molecular weight tell you as a preclinician?
A. It gives a measure of the stability of the polymer.
Q. If the molecular weight changes, what happened to the polymer?
MR. THORNBURGH: Objection. Outside the scope of his expertise.
He's already testified at length that he's not a polymer scientist. I've already asked him these questions, and he couldn't give me answers to them.
MR. THOMAS: I don't think you asked that question.
But go ahead.
MR. THORNBURGH: I did.
THE WITNESS: Could you repeat, David?
BY MR. THOMAS:
Q. What does the change in molecular weight tell you as a preclinician?

Page 621

A. A change in molecular weight is --
MR. THORNBURGH: Same objection. I'm sorry.
THE WITNESS: -- is a quantitative measure. That would suggest it's quite reliable. And it would be a measure of degradation of the polymer.
BY MR. THOMAS:
Q. And what is tensile strength?
A. Tensile strength is the force required to break a fiber, in a -- in a brief description.
Q. And why is a loss of tensile strength important to you as a preclinician?
A. Tensile strength is a measure of fiber integrity. It's a measure of presence or absence of degradation.
And for suture, it's critical, because if a suture breaks because of a loss of tensile strength, it can have very serious consequences for patients when used for cardiovascular repair.
And if there is a loss of strength of fiber and in mesh, there could be a reduction in burst strength of the mesh, and so that it doesn't

Page 622

perform its function as intended.
Q. On Exhibit 2264, which is the October 15, 1992 report titled, "Seven-Year Data For Ten- Year Prolene Study," ERF-85-219, down under the paragraph headed "IV and GPC," it says: Gel permeation chromatography (GPC) was run on Prolene sutures explanted from dogs after seven years. The GPC data was compared to data from a current 4/0 Prolene suture.
What does that mean?
A. 4/0 suture was the suture size that was implanted in the dogs. And so to make a relevant comparison, they selected a 4/0 suture out of package to make the comparisons.
Q. Okay. The results indicate there was no significant difference in molecular weight between the 4/0 Prolene suture and the seven-year explants.
What significance of that -- is that to you as a preclinician?
MR. THORNBURGH: Objection.
THE WITNESS: That is strong evidence that there's no polymer degradation taking place.
BY MR. THOMAS:
Q. Turn now, please, to Exhibit 2263.

Page 623

MR. THORNBURGH: What page is that? I'm sorry.
MR. THOMAS: Exhibit 2263.
BY MR. THOMAS:
Q. If you go to the last three pages of Exhibit 2263, there is a document titled -- dated October 19, 1992.
And it says: Interim report on the physical testing of Prolene, PVDF, Ethilon, and Novofil after seven-year subcutaneous implantation in the Beagle dogs.
Do you see that?
A. Yes.
Q. And what is a BSR study?
A. BSR is an acronym that stands for breaking strength retention.
Q. And how does breaking strength retention compare to tensile strength?
A. Breaking strength retention would be determined by tensile testing.
Basically, they would look at out of package suture and do tensile testing to determine breaking strength. And then they would explant suture from these dogs after seven years and do similar tensile testing and make a comparison.

Page 624

Q. And in 1992, tests were conducted, and it reads here: The attached table shows the physical properties of explanted and baseline samples of size 5/0 Ethilon, Novafil, Prolene, and PVDF (N) sutures up to the seven-year mark of the ten-year BSR study.
Reading further, it says: Novofil samples show a corresponding decrease of 14 percent in breaking strength, while Prolene and PVDF show no significant change after seven years of implantation.
What's the significance of that finding to a preclinician in evaluating the stability of Prolene sutures?
MR. THORNBURGH: Objection.
THE WITNESS: That's strong evidence that there's no degradation of the polymer fiber.
BY MR. THOMAS:
Q. If you go back to Pages Bates Number 09888218, which is going back from the back -- it's a few pages in from the back.
A. Okay.
Q. Do you have that?
A. Yeah.
MR. THORNBURGH: I am not there yet.

Page 625

I'm sorry. What was the last?
MR. THOMAS: The analytical chemistry department notes. The last two numbers are 218.
MR. THORNBURGH: Got it.
BY MR. THOMAS:
Q. And do you understand these to be notes taken in the analytical chemistry department for testing conducted on these mesh -- these suture explants?
A. Yes.
Q. And down to the bottom of the page, it says: Prolene site one and Prolene site six with molecular weights of 322,000 and 323,000 compared to a molecular weight of 324,000.
What is the significance of that to you as a preclinician?
MR. THORNBURGH: Objection.
THE WITNESS: The polymer is not showing any significant changes in molecular weight. And as the comments indicate below, a comparison -- and this is a summary of that molecular weight data.
A comparison of seven-year explants to current 4/0 Prolene sutures indicates no significant degradation.
BY MR. THOMAS:

Page 626

Q. And that's dated October 9, 1992, down in the lower left by Eugene Muse.
A. Yes. October 9, 1992.
Q. If you turn the page and go to 220.
A. Okay.
Q. And 220 is a document dated September 21, 1992. The analyst's signature, it looks like Robin Ragland, and comparing, again, Prolene sutures for dog 1995 site three. Do you see that?
A. Yes.
Q. And the Prolene suture for dog 1995, site three, was compared to a current Prolene suture 4/0.
Again, what's going on here?
A. Yeah. This is a comparison of the molecular weight of the suture from explant compared to a current Prolene suture.
And the results indicate, as is stated, that no degradation has taken place. And that's fully supported by the quantitative molecular weight data. Those -- that statement and that data is very consistent.
Q. And you go to the next page, which is 8221, dated August the 5th, 1992, Dan Burkley,

Page 627

signed off by Gene Muse, on October 9, 1992.
Again, they're comparing Prolene suture explants for Dog 2019, site two and three, to the current Prolene control. Is that correct?
A. Yes.
Q. And they're comparing molecular weights again?
A. Yes.
Q. And what conclusion do they reach in October -- in August 1992 about degradation with respect to these suture implants?
A. For samples from this dog, they say in the conclusion section: Comparison of seven-year explants to current Prolene indicate no molecular weight degradation.
Q. And the next page dated 8222 -- excuse me -- numbered 8222, again, is submitted July 2, 1992.
A. Okay.
Q. I am trying to find my Prolene.
Here it is. In the middle?
A. Yep.
Q. There's Dog 2008, site two?
A. Yes.
Q. Measure of molecular weight, again,

Page 628

compared to the control. Do you see that?
A. Yes.
Q. And what conclusion is reached in 1992 about Dog 2008?
A. For this dog, they're saying comparison of current Prolene 4/0 suture indicates no significant degradation of seven-year explant.
Q. Now, we talked before and went through in great length about the surface cracking that was reserved in the scanning electron microscopy. I don't need to go through that again in any detail unless you want to.
A. No thanks.
Q. But how can you reconcile what was found as a preclinician, the findings of the scanning electron microscopy with the molecular weight tensile strength results that are recorded here?
A. The surface changes are informational. However, in my mind as a preclinical scientist, they're not having an adverse impact on molecular weight or tensile strength of the fiber.
Q. And what importance as a clinician is that conclusion to you?
A. Well --

Page 629

Q. Excuse me. I'm sorry. I have misspoken. Strike that.
What importance as a preclinician is that conclusion to you?
MR. THORNBURGH: Objection.
THE WITNESS: I think it demonstrates the stability of Prolene suture over seven years in in vivo -- in in vivo system.
BY MR. THOMAS:
Q. Do any of the documents, the study for the seven-year dog study where there is a discussion of these surface cracks on some of the explanted sutures in some of the locations -- is there any attribution of cause to that cracking?
MR. THORNBURGH: Objection.
THE WITNESS: It's simply an observation.
MR. THOMAS: Can we take a break, please.
THE VIDEOGRAPHER: Off the video record, 6:55.
(Short break.)
THE VIDEOGRAPHER: Back on the video record at 7:00 p.m.
MR. THOMAS: I have no further

Page 630

questions.
- - -
FURTHER EXAMINATION
- - -
BY MR. THORNBURGH:
Q. Doctor, I appreciate that we've all been here too long today and we're all tired. I do have a couple of questions. I'm going to try to get us all out of here as quickly as I can. Okay?
I want to kind of work backwards. I want to turn your attention back to the seven-year dog study, which I think was Exhibit Number 2264, which included the analytical chemistry department notes.
MR. THOMAS: 2263, I think.
MR. THORNBURGH: Is it 2263?
THE WITNESS: Okay.
BY MR. THORNBURGH:
Q. Now, there actually was molecular weight loss in some of the cracked -- or some of the explanted Prolene sutures, wasn't there?
A. There was no significant changes.
Q. There was -- answer my question. Okay? Because I know we both want to get out of here. So answer my question.

Page 631

There actually was molecular weight loss in some of the explanted Prolene sutures, wasn't there?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Let's look at the data. I don't recall the specifics.
BY MR. THORNBURGH:
Q. Let's turn to ETH.MESH.09888222.
A. 232.
232.
Q. Yes. No. 09888222.
A. 222.
Q. Are you there?
A. Yes.
Q. Dog 2008, site two, was compared to current Prolene 4/0 suture, right?
A. Yes.
Q. And the current Prolene suture had a molecular weight of 224,000, and an MN of 60,000, right?
MR. THOMAS: Object to form. You read that wrong.
THE WITNESS: No. I think it's 324,000.

Page 632

BY MR. THORNBURGH:
Q. 324,000?
A. For MW. And 60,000 for MN.
Q. Molecular weight was 324,000, correct?
A. Yes.
Q. What does MN mean, by the way?
A. It is a measure of the number of molecular chains versus the average molecular weight of those chains.
Q. For molecular weight, there was a reduction of the Prolene, current Prolene, compared to the dog explant suture, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: The number is different, and it's lower.
BY MR. THORNBURGH:
Q. It's lower in the explanted Prolene, correct?
A. Yes, at this site.
Q. And you said the MN was the number of molecular chains?
A. Yes, in a general way. Again, I'm not a polymer chemist, but that's my understanding.

Page 633

Q. There was a change in the number as well, wasn't there, Doctor?
A. I wouldn't expect these numbers to come out on top of each other.
Q. 60,000 in the current Prolene versus 53,000 in the explanted Prolene, correct?
A. That's what it says.
Q. That would indicate there was a reduction in the number of polymer chains, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Well, the conclusion says no significant degradation of the seven-year explant.
BY MR. THORNBURGH:
Q. Right. The conclusion isn't that there was no degradation; the conclusion is there wasn't significant degradation. But the converse is true, that there was evidence of some degradation, wasn't there, Doctor?
MR. THOMAS: Object to the form of the question.
THE WITNESS: What's important to me as a preclinical scientist is what the person doing the work interprets the results and gives a final

Page 634

conclusion.
I know that these molecular weight numbers can never be identical between samples, because there is a range of molecular weights.
BY MR. THORNBURGH:
Q. Answer my question, please, Doctor.
MR. THOMAS: I think he did.
BY MR. THORNBURGH:
Q. The finding here was that there was a reduction in molecular weight, and there was a reduction in the molecular molecules, and that there was some degradation observed of this explant, explanted mesh, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: These are two numbers. These numbers need to be interpreted.
BY MR. THORNBURGH:
Q. You can't interpret those numbers?
A. They have been interpreted for me as I read this report.
Q. And there was indication of degradation, wasn't there?
A. The conclusion say that no significant degradation of a seven-year explant.

Page 635

Q. Which doesn't mean that there wasn't degradation; it just means that there was degradation but this investigator called it insignificant or not significant. Right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: I would disagree.
BY MR. THORNBURGH:
Q. If we go to -- that's what the summary is for, too, right, Doctor? Summaries in reports authored by the investigators is to help us understand their interpretation of the data?
A. Absolutely.
Q. And if we look at the summary of the conclusions -- which are a summary of the data, right? It's a conclusion of the --
A. What page are you on?
Q. I am looking at Page 2 of --
MR. THOMAS: Dan, just so you know, the full page that talks about molecular weight is 2264. The copy that you have is folded over. I gave you a copy of that already.
MR. THORNBURGH: I don't know what I did with the full page. What is the exhibit number?
MR. THOMAS: 2264.

Page 636

BY MR. THORNBURGH:
Q. If we look at 2264.
A. 2264, yes.
Q. Strike that. Let me just try to see if I can get a clean answer from you, get a clean record.
You would agree with me that as a scientist, you rely on the conclusions of the investigators who conducted the study, right?
A. Yes, in large part.
Q. And the conclusion from the investigator who conducted this study was that there was --
A. What page are we on now?
Q. If we look at page -- it's Page 2 of the expert report.
A. The ETH.MESH. number?
Q. 2264.
MR. THOMAS: Object. Who do you attribute to be the investigator? There's three, I believe.
MR. THORNBURGH: The person who wrote the report.
MR. THOMAS: There are three.
BY MR. THORNBURGH:

Page 637

Q. There's three -- three folks that signed the report, right?
A. I'm still looking for the summary. I can't find it.
Q. If you look at Exhibit Number 2264.
MR. THOMAS: Over there in that stack right there.
THE WITNESS: Okay.
BY MR. THORNBURGH:
Q. Okay. And three -- not one Ethicon employee or Ethicon investigator signed this report, but three of them signed the report, right?
A. Yes.
Q. Which -- and in the report, their conclusions, the three Ethicon employees who actually participated in the study, their conclusions was that there was degradation in the polypropylene, in the Prolene, right?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. That's their conclusion in the report?
MR. THOMAS: Object to the form of the question.

Page 638

BY MR. THORNBURGH:
Q. I'm not -- I am not misreading this right, Doctor?
MR. THOMAS: I think you are, Dan.
BY MR. THORNBURGH:
Q. Conclusion. Degradation in Prolene is still increasing, and PVDF, even though a few cracks were found, is still by far the most surface resistant in-house made suture in terms of cracking.
I read that correctly, didn't I, Doctor?
MR. THOMAS: Object to the form of the question.
THE WITNESS: This is a conclusion for the ophthalmic microscopy and scanning electron microscopy section authored by the Elke Lindemann, the person who did the SEM evaluation.
BY MR. THORNBURGH:
Q. And the conclusion, which was signed off on by three Ethicon employees who -- scientists, polymer scientists, right?
A. Each of the scientists --
Q. Answer that question first, please.
A. Each of the scientists' names are against the part of the report for which they signed

off.
Q. Three of them participated in the study, right?
A. That's correct.
Q. And the conclusion on Page 2 says: Degradation in Prolene is still increasing, and PVDF, even though a few cracks were found, is still by far the most surface resistant in-house made suture in terms of cracking. Right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: That's one-third of the results of this experiment.
BY MR. THORNBURGH:
Q. Well, is that one-third of the results of the experiment -- in the experiment, they determined that there was degradation, there was surface degradation of the Prolene mesh, right?
A. That's what it says.
Q. Or Prolene suture.
And we can see there was a loss in molecular weight seen on this explant, right?
A. Let me get to that section. 222, is that the --
Q. Yes.

A. Okay. I'm looking at it.
Q. It doesn't say that there wasn't degradation, does it?
A. Well, I -- let's take a look at all the other dogs and see what happened.
Q. Well, I know you don't want to talk about the evidence that's not good for Ethicon, but we got to talk about that evidence, too, Doctor.
MR. THOMAS: Excuse me. Stop, stop. Just ask a good question. Don't argue with him.
MR. THORNBURGH: It was a good question.
MR. THOMAS: Come on. Stop.
MR. THORNBURGH: It was a good question. I'm not making fun of the doctor.
MR. THOMAS: Do you want to quit? We'll quit.
MR. THORNBURGH: No. That was a good question.
MR. THOMAS: That's ridiculous.
MR. THORNBURGH: He didn't want to answer it because -- because he didn't want -- he didn't want the truth to be heard.
MR. THOMAS: I want you to argue that one to the magistrate, to the judge.

MR. THORNBURGH: What do you mean?
MR. THOMAS: Just what I said.
THE WITNESS: I am looking at Animal 1995.
BY MR. THORNBURGH:
Q. So hold on a second. Let's talk about Animal 2008, site two.
There was a reduction --
MR. THOMAS: You can do them one at a time, Tom. You can do them one at a time. If he won't ask you, I'll ask you.
THE WITNESS: Fine. Okay.
MR. THORNBURGH: I'll look at all of them.
THE WITNESS: Fine.
MR. THORNBURGH: I am not afraid of the evidence.
THE WITNESS: Me neither.
BY MR. THORNBURGH:
Q. There is a reduction in the molecular weight and the number of molecules, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: The number is smaller. The conclusion is that there's no significant

degradation.
BY MR. THORNBURGH:
Q. Oh, by the way, did you talk to these investigators about why there was insufficient sample for Prolene IV for this study?
A. No, I did not.
Q. Did you talk to the investigator --
A. What are we looking at now?
Q. Same page, 222.
A. 222. Insufficient sample for inherent viscosity, not molecular weight.
Q. Insufficient Prolene -- sorry. Insufficient sample for Prolene IV. Right. That's what that says?
A. No. No. It's IV which means inherent viscosity.
Q. What is inherent viscosity?
A. It's another measure of polymer characteristics. It's different than a molecular weight measurement.
Q. And that's why it's not included in here, right?
MR. THOMAS: Included where?
MR. THORNBURGH: Included right below for the --

Page 643

BY MR. THORNBURGH:
Q. I assume -- and you can tell me -- you can answer the question for me, if you can.
The IV results --
MR. THOMAS: They're above, Dan.
MR. THORNBURGH: Hold on one second.
BY MR. THORNBURGH:
Q. Is this the IV results here?
A. IV/DLG, that is an IV result.
Q. Okay. I'm sorry.
A. They're saying they could not -- there was insufficient sample to determine an IV measurement for Prolene suture.
Q. And what is an IV measurement?
A. It represents inherent viscosity, again, a measure -- it's a polymer characteristic.
Q. Would it give us information about the loss of the polymer?
A. I don't know for certain. I think it's a different endpoint, but I don't know for certain.
Q. In any case, they're able to test all of the other samples except for Prolene for that study, right, for IV?
A. That's what it says, yes.

Page 644

Q. If you go to 8221.
MR. THOMAS: Do you want to ask the rest of the questions about the molecular weight down at the bottom of that page?
MR. THORNBURGH: I see Prolene wasn't included in that -- in this section of molecular weight. Right?
MR. THOMAS: Oh, I think it is.
THE WITNESS: No. That's IV. Molecular weight is above to the right.
BY MR. THORNBURGH:
Q. Okay. I'm sorry.
A. So --
Q. What's this -- what's this data right here?
A. That's -- that's molecular weight data for the other suture -- sutures.
Q. Okay. And the molecular weight data here we've already discussed, which showed a reduction in the molecular weight from the current Prolene to the explant and, also, a reduction in the number of molecules, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: The numbers are

Page 645

different, and the Dog 2008 site two is a smaller number.
MR. THORNBURGH: Is that the section that you wanted me to go back to and ask questions about?
MR. THOMAS: You can ask whatever you want to. I'm not going to tell you what to do.
BY MR. THORNBURGH:
Q. If you go to 8221.
A. 8221. Okay.
Q. There was insufficient sample of Prolene for IV again, right?
A. That's correct.
Q. Then, also, again, insufficient sample of Prolene IV again here, right? You see it says insufficient Prolene IV. And then it also says insufficient Prolene IV here. And it doesn't give numbers for the Prolene.
MR. THOMAS: It does at the bottom. Current molecular weight right there on the bottom.
MR. THORNBURGH: We're going to talk about that -- we're going to talk about that in a moment.
MR. THOMAS: I thought you were suggesting --

Page 646

BY MR. THORNBURGH:
Q. Because right here, they separate it out, right? In both cases, it says insufficient sample for Prolene IV.
A. That is just written twice.
Q. Do you know why there would be insufficient samples for Prolene IV?
A. No, I do not. I know you need to have a certain mass in order to do the experiment. And the analytical work was done on the strand breaks after Instron testing. So maybe there was just not enough mass to run the experiment, a certain sample requirement.
Q. And for molecular weight, current Prolene, there's -- the explants in this sample were also lower than the -- than the control, correct?
MR. THOMAS: Object to the form of the question. That's not true.
THE WITNESS: No, that's not correct.
BY MR. THORNBURGH:
Q. 334,000 --
MR. THOMAS: No.
BY MR. THORNBURGH:
Q. -- is greater than 331,000.
MR. THOMAS: You're not reading the

Page 647

number right, Dan. It's 324,000.
MR. THORNBURGH: Oh, okay. I'm apparently dyslexic today.
BY MR. THORNBURGH:
Q. So there was -- in this -- in this sample, there wasn't degradation observed, molecular degradation, right?
A. Well, to use your language from the previous dog, there were increases in molecular weight for two strands.
Q. There wasn't molecular weight degradation; there wasn't a decrease in the molecular weight seen in this sample. Right?
A. There was an increase.
Q. There wasn't a reduction in -- there wasn't -- look at the conclusion.
The conclusion was no molecular weight degradation, right?
A. That's right.
MR. THOMAS: That's fine.
THE WITNESS: That's right.
BY MR. THORNBURGH:
Q. Molecular weight degradation. That's what they call it here, right?
A. That's right. What this is

Page 648

suggesting is that molecular weight rises and falls in comparison to a control, and the investigator needs to make a judgment whether or not the movement from the baseline is sufficient to call out significant degradation. That's how science works.
Q. Again, there's insufficient sample for Prolene IVs, right?
MR. THOMAS: What page are we on now?
MR. THORNBURGH: 8220.
THE WITNESS: Yes. Insufficient sample for the IV test.
BY MR. THORNBURGH:
Q. Why -- why is -- why is -- why are these researchers able to run IV testing on all other sutures except for Prolene?
A. I don't know the answer for that.
Q. Did you ask anybody?
A. No.
Q. In every single case, they didn't run a test for Prolene IV, right?
A. For me, the molecular weight determination was the most relevant. It may be because I understand it a little bit better than IV.
Clearly, IV is an important measurement, but -- maybe someone else can address

Page 649

the significance of that in polymer science, but I can't shed much light on it.
Q. You didn't talk to anybody, right?
A. That's correct.
Q. You didn't call up Dan Burkley or the other two investigators and say, hey, why is there -- why weren't you able to do Prolene IV studies?
A. That's correct.
Q. So the people most knowledgeable about that -- that particular issue in this study wouldn't include you; it would include somebody else?
A. At this level of detail, yes.
Q. It would appear, though, that IV had analysis -- is related in some way to a degradation analysis, right?
MR. THOMAS: Object to the form of the question.
THE WITNESS: No, I don't think so.
MR. THORNBURGH: We'll mark as Exhibit 2265.
(Document marked for identification as Exhibit T-2265.)
BY MR. THORNBURGH:

Page 650

Q. A degradation analysis of Prolene explants.
MR. THOMAS: Where did this come from?
MR. THORNBURGH: This is --
MR. THOMAS: A lab notebook?
MR. THORNBURGH: I believe so, yes.
MR. THOMAS: We've already told you that we're not prepared.
MR. THORNBURGH: You're not prepared to talk about --
BY MR. THORNBURGH:
Q. You haven't seen this?
A. I have not seen this.
Q. Do you see the date on this?
MR. THORNBURGH: If he's not prepared to tell me or talk about it, then he needs to say I'm not prepared to talk about it. I'm going to ask one or two questions.
MR. THOMAS: We're not. We're not prepared to talk about it.
THE WITNESS: I haven't seen it.
BY MR. THORNBURGH:
Q. Do you know what melt pointing is, melt point test?

Page 651

A. No. I can't explain that in any detail.
Q. Nobody at Ethicon provided you with this study that showed that in 1987, the explants showed that there -- the conclusions from studies of explants was that it was degraded Prolene?
MR. THOMAS: Object to the form of the question. He's not prepared to talk on this. We've been through this at length.
BY MR. THORNBURGH:
Q. My question is: Nobody at Ethicon, nor Ethicon's counsel, provided you with this study that showed the explanted Prolene was degraded?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. Right?
A. I've not seen this. I am not really -- I'm not prepared to talk about it. It is a bit of information in isolation. I don't understand the context. I'd have to look at all -- at all the data around it.
Q. Nobody -- nobody showed you this conclusion either, or this study either, prior to coming here today, a study that they've had

Page 652

apparently in Ethicon's files since 1987, which showed that the explanted meshes -- the explant mesh --
MR. THOMAS: Are you referring to something new? Or is this the same document?
MR. THORNBURGH: Same document.
THE WITNESS: It's a notebook page.
BY MR. THORNBURGH:
Q. Nobody showed you this document either?
A. It's a notebook page.
Q. Nobody showed you the study results from Professor Godoin? Professor Godoin. Nobody showed you Professor Godoin's explants and the studies that were done on Professor Godoin's explants which showed evidence of polypropylene degradation?
MR. THOMAS: Object to the form of the question.
THE WITNESS: If there's anything in any notebooks that you want to talk about, I'm not prepared to talk about it.
BY MR. THORNBURGH:
Q. Yeah. So nobody showed you this study, right? Nobody at Ethicon, nor Ethicon's

Page 653

attorneys -- Ethicon has been in possession of this since 1987 -- did not provide this information to you, correct?
A. I have not seen this information.
Q. So you're not prepared to talk about that study or any other studies from the notebooks?
MR. THOMAS: We've already said that a hundred times.
MR. THORNBURGH: We'll have to come back.
MR. THOMAS: I understand.
BY MR. THORNBURGH:
Q. Now, you represented that there were 20 binders in front of you and behind you which included studies that you -- that Ethicon -- Ethicon's attorneys and you compiled together for purposes of this deposition, right?
A. Yes.
Q. And you -- you have to agree that many of the studies that were copied and put in these binders are actually duplicates of studies in other binders in front of you, right?
A. That's correct.
Q. Many of them, a vast majority of them?

Page 654

A. That's correct.
Q. It's not actually 20 binders of different studies. There's 20 binders where the majority of those are duplicate copies, right?
A. I never represented them as individual lists of studies that were not duplicates.
Q. I just want to make sure the jury understands. It's not actually 20 binders of studies, of different studies. There's 20 binders with lots of duplication, right?
A. Yes. There's overlap between the topics of discussion.
Q. In fact, some studies are contained within -- are duplicated 10 and 11 times in these binders, right?
A. I don't think there were that many topics for discussion.
Q. Or duplicated in each one of the topics?
A. Okay.
Q. Right? Correct?
A. That could be so.
Q. Exhibit 2262, the list of studies.
A. Okay.

Page 655

Q. Now, we've marked that as an exhibit. Do you have it in front of you?
A. Yes.
Q. Okay. You have a list of studies and -- that you included or somebody included in the degradation section of Exhibit 2262, correct?
A. Yes.
Q. And can you tell me in exhibit -- or in Study Number 1, study of tissue reaction of colorless and pigmented monofilament polypropylene sutures, was there SEM, SEM EDX, GPC, DTP, or FTIR studies conducted?
A. No.
Q. And to determine if there was actually actual degradation of the polypropylene in these cases, a number of studies would have to be conducted, right? A number of tests?
A. Not necessarily. One can determine quite a bit by looking at the tissue reaction from an implanted material and whether or not there's any evidence that there's cracking, degradation, absorption, edge -- edge erosion.
Q. SEM -- SEM --
MR. THOMAS: Excuse me.
BY MR. THORNBURGH:

Page 656

Q. I'm sorry. I thought you were done. I didn't mean to interrupt you.
A. It's all right. I'm done.
Q. I see the period. Now -- or I hear the period.
Doctor, are you telling the ladies and gentlemen of the jury that SEM analysis alone is sufficient to determine degradation or surface degradation of a polymer fiber?
A. Absolutely not.
Q. Additional testing could be conducted, right?
A. Yeah, as was done in the seven-year dog study.
Q. You said that -- you testified a moment ago that one can determine the tissue reaction from implanted material and whether or not there's any evidence that there's cracking, degradation, absorption, edge erosion.
So I am going to break that down for a moment. Okay?
A. Okay.
Q. So one can determine through light microscopy or SEM surface cracks, correct?
A. As was done in the seven-year dog study.

Page 657

Q. Okay. And then you have degradation here, which could include surface degradation, correct?
A. If it were significant enough to be seen at the light microscope level in an H&E section, yes.
Q. What do you mean by absorption?
A. For absorbable implants, there's an absorption of the material into the surrounding tissues. That's not the case for a non-absorbable, which is Prolene.
Q. And what do you mean by "edge erosion"?
A. There might be degradation of the surface which would be reflected by inflammatory cells scalloping the perimeter of the implant, fiber.
Q. Now, for these studies that you listed here in degradation, the overwhelming majority of these studies weren't studies that looked at FTIR analysis, scanning electron microscopy, scanning electron microscopy EDX, GPC, or those other tests, degradation tests, correct?
MR. THOMAS: Object to the form of the question.
THE WITNESS: Yes.
BY MR. THORNBURGH:
Q. In fact, can you point to any of these studies that you have listed in the degradation section of your -- your notebooks that did FTIR microscopy?
A. Seven-year dog study.
Q. That's it? That's the only one that you can point to, right?
A. Yes.
Q. And the seven-year dog study through FTIR found degradation, correct?
MR. THOMAS: No. Object to the form of the question.
BY MR. THORNBURGH:
Q. There were carbonyl bands that were consistent with oxidation, correct?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. Correct?
A. I recall some language about a possibility of such a thing, but nothing definitive.
Q. There were carbonyl bands that were

Page 658

Page 659

seen that were consistent with oxidation, according to the report.
MR. THOMAS: Object to the form of the question.
THE WITNESS: No, they -- we can go to the report and look.
BY MR. THORNBURGH:
Q. Okay.
MR. THOMAS: It's on Page 1, I believe.
THE WITNESS: There would be an ETH.MESH.09888187, whereas I have recalled the statement says, showed possible evidence of slight oxidation.
BY MR. THORNBURGH:
Q. So the only study that you listed in your 40 some studies that actually did FTIR microscopy found that the IR spectra obtained for cracked Prolene specimens showed possible evidence of slight oxidation, correct?
A. I think I just said that.
Q. Correct?
A. Yes.
Q. The only study that you listed in your degradation study -- or degradation list of

Page 660

studies that actually did FTIR microscopy showed evidence of degradation.
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. Right?
MR. THOMAS: Object to the form of the question.
BY MR. THORNBURGH:
Q. Right, sir?
A. Can you restate?
Q. Yeah. Yeah. And I can try to ask in a better way.
The only study that you can identify right now for the ladies and gentlemen of the jury in your list of degradation studies on Exhibit 2262 that actually looked at FTIR microscopy found evidence of oxidation and degradation, correct?
MR. THOMAS: Object to the form of the question. Read it correctly, please.
MR. THORNBURGH: Read it correctly? I wasn't reading anything.
MR. THOMAS: Read what the report says.
MR. THORNBURGH: There is evidence

Page 661

of -- listen. I am summarizing.
The only study -- listen, Dave. I would appreciate if you would stop coaching this witness.
MR. THOMAS: I am not coaching the witness.
MR. THORNBURGH: You are. You have been coaching him for the last two days, Dave. I don't do that to you.
MR. THOMAS: Stop, please.
MR. THORNBURGH: I have respect for you. I treat you like a professional.
MR. THOMAS: I bet you do.
MR. THORNBURGH: You don't treat me like a professional. You don't act professional when I am asking questions. You coach the witness.
BY MR. THORNBURGH:
Q. The only study that you listed in your degradation section of the studies that were compiled by you or someone for Ethicon or Ethicon's attorneys say -- show -- showed evidence of -- possible evidence of oxidation and degradation, right?
A. We've discussed this line several times today.

Page 662

Q. And the answer is yes, correct?
A. It showed possible evidence of slight degradation. What's written is undeniable.
THE WITNESS: I am hoping to wrap this up soon, Dave. I am running out of steam.
MR. THOMAS: I understand.
Just in light of what he said, are you getting close to being finished?
MR. THORNBURGH: Yeah. I got -- I only have a few little notes here.
MR. THOMAS: Well, last time that got a little bit too late, and the witness is getting tired. I'm just trying --
THE WITNESS: I'm getting tired. And if you've got a lot of questions to ask --
MR. THORNBURGH: I'm tired, too. I'm tired, too.
THE WITNESS: -- and if it's going to go beyond five minutes, we need to schedule more time.
MR. THORNBURGH: I'm tired, too, Doctor.
MR. THOMAS: Let's go. Let's go.
BY MR. THORNBURGH:
Q. You're getting paid for your time

today, aren't you?

A. Like I said, you've got five minutes. I am running out of energy. If you need more time, we'll have to reschedule more time.

Q. How much money are you getting paid by the hour by Ethicon to come in here and testify as a 30(b)6 witness?

A. You know that it's $225 an hour. You've asked me before. And that's the same reason I gave --

MR. THOMAS: Whoa, whoa, whoa. Just relax. Just don't -- you're asking questions over and over again. Let's ask the questions and move on.

MR. THORNBURGH: I hear you. I know you're tired. I am going to pass the witness.

MR. THOMAS: Thank you. That's all we have. Thanks very much.

THE VIDEOGRAPHER: It's now 7:33, and we're concluded with Tape Number 6 in the videotape deposition of Thomas A Barbolt.

(Witness excused.)

(Deposition concluded at approximately 7:33 p.m.)

CERTIFICATE

I HEREBY CERTIFY that the witness was duly sworn by me and that the deposition is a true record of the testimony given by the witness.

It was requested before completion of the deposition that the witness, THOMAS A. BARBOLT, Ph.D., have the opportunity to read and sign the deposition transcript.

____

MICHELLE L. GRAY, a Registered Professional Reporter, Certified Shorthand Reporter and Notary Public
Dated: January 16, 2014

(The foregoing certification of this transcript does not apply to any reproduction of the same by any means, unless under the direct control and/or supervision of the certifying reporter.)

INSTRUCTIONS TO WITNESS

Please read your deposition over carefully and make any necessary corrections. You should state the reason in the appropriate space on the errata sheet for any corrections that are made.

After doing so, please sign the errata sheet and date it. It will be attached to your deposition.

It is imperative that you return the original errata sheet to the deposing attorney within thirty (30) days of receipt of the deposition transcript by you. If you fail to do so, the deposition transcript may be deemed to be accurate and may be used in court.

\- - - - - -
E R R A T A
\- - - - - -

PAGE LINE CHANGE

____ ____ ________________________
REASON ________________________
____ ____ ________________________
REASON ________________________
____ ____ ________________________
REASON ________________________
____ ____ ________________________
REASON ________________________
____ ____ ________________________
REASON ________________________
____ ____ ________________________
REASON ________________________
____ ____ ________________________
REASON ________________________
____ ____ ________________________
REASON ________________________
____ ____ ________________________
REASON ________________________
____ ____ ________________________
REASON ________________________
____ ____ ________________________
REASON ________________________

ACKNOWLEDGMENT OF DEPONENT

I,____________________, do hereby certify that I have read the foregoing pages, 294 - 668, and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

____

THOMAS A. BARBOLT, Ph.D. DATE

Subscribed and sworn
to before me this
_____ day of ______________, 20____.
My commission expires:______________

____

Notary Public

LAWYER'S NOTES

PAGE LINE

____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________
____ ____ _________________________________

U